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Barb O'Bryen

70697

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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Rebecca Cook (STIC) Examiner # : _____ Date: 7/11/02

Art Unit: 1614 Phone Number 30 5 4722 Serial Number: 10/380059

Mail Box and Bldg/Room Location: CM1 2D01 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): Hiroyuki Odaka

M Yamane

Earliest Priority Filing Date: 6/30/98

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

1. Please search method for determination of concentration of glycosated hemoglobin using immunoassay + an annotation. (see cl 1)

2. using glycosated hemoglobin control +/or diabetes control.

3. structures 1/ compounds of Claims 3, 6, 1, 2 4.

Thanks!
Rebecca

Point of Contact:
Barb O'Bryen
Technical Information Specialist
STIC CM1 6A05 308-4291

****

STAFF USE ONLY

Searcher: BOB

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: 7-22-02

Searcher Prep & Review Time: 40

Clerical Prep Time: _____

Online Time: 112

Type of Search

NA Sequence (#) _____

AA Sequence (#) _____

Structure (#) _____

Bibliographic X

Litigation _____

Fulltext _____

Patent Family _____

Other _____

Vendors and cost where applicable

STN 451

Dialog _____

Questel/Orbit _____

Dr.Link _____

Lexis/Nexis _____

Sequence Systems _____

WWW/Internet _____

Other (specify) Chem Draw

PTO-1590 (8-01)

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=> fil reg
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STRUCTURE FILE UPDATES:   21 JUL 2002  HIGHEST RN 439659-64-0
DICTIONARY FILE UPDATES:  21 JUL 2002  HIGHEST RN 439659-64-0

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide

L4   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   111025-46-8  REGISTRY
CN   2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-
      (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-
     , (.+-.)-
OTHER NAMES:
CN   59: PN: WO0148150 SEQID: 74 claimed sequence
CN   Pioglitazone
CN   U 72107
FS   3D CONCORD
DR   105355-27-9, 198077-89-3
MF   C19 H20 N2 O3 S
CI   COM
SR   US Adopted Names Council
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*,
       BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB,
       CEN, CHEMCATS, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES,
       EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN,
       USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   WHO
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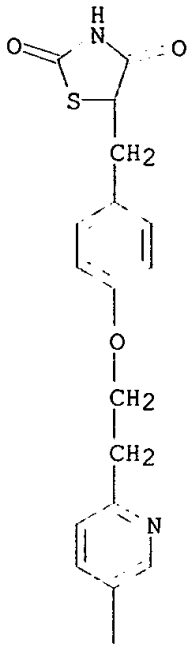
PAGE 1-A



PAGE 2-A

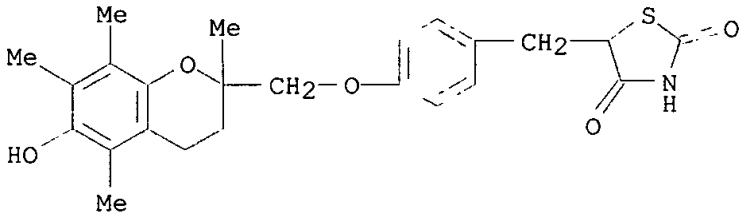
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

382 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
387 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d ide

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 97322-87-7 REGISTRY
CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 58: PN: WO0148150 SEQID: 73 claimed sequence
CN CI 991
CN CS 045
CN GR 92132X
CN Noscal
CN Rezulin
CN Romglizone
CN **Troglitazone**
FS 3D CONCORD
DR 259223-65-9
MF C24 H27 N O5 S
CI COM

SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

820 REFERENCES IN FILE CA (1967 TO DATE)
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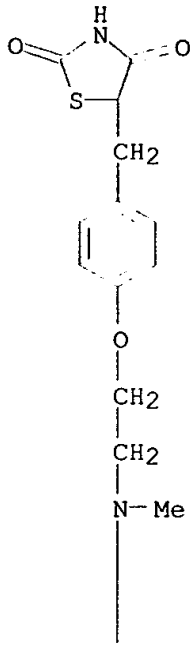
825 REFERENCES IN FILE CAPLUS (1967 TO DATE)

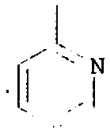
=> d ide

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 122320-73-4 REGISTRY
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 60: PN: WO0148150 SEQID: 75 claimed sequence
CN BRL 49653
CN **Rosiglitazone**
FS 3D CONCORD
MF C18 H19 N3 O3 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

PAGE 1-A



PAGE 2-A



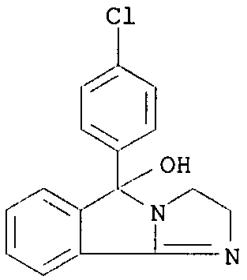
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

429 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
433 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d ide

L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 22232-71-9 REGISTRY
CN 3H-Imidazo[2,1-a]isoindol-5-ol, 5-(4-chlorophenyl)-2,5-dihydro- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3H-Imidazo[2,1-a]isoindol-5-ol, 5-(p-chlorophenyl)-2,5-dihydro- (8CI)
OTHER NAMES:
CN 5-(4-Chlorophenyl)-2,3-dihydro-5-hydroxy-5H-imidazo[2,1-a]isoindole
CN 5-(p-Chlorophenyl)-2,3-dihydro-5H-imidazo[2,1-a]isoindol-5-ol
CN 5-(p-Chlorophenyl)-2,5-dihydro-3H-imidazo[2,1-a]isoindol-5-ol
CN 5-(p-Chlorophenyl)-5-hydroxy-2,3-dihydro-5H-imidazo[2,1-a]isoindole
CN 5-Hydroxy-5-p-chlorophenyl-2,3-dihydro-5H-imidazo[2,1-a]isoindole
CN AN 448
CN **Mazindol**

CN SaH 42548
CN Sanorex
CN Teronac
FS 3D CONCORD
MF C16 H13 Cl N2 O
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, DDFU, DIOGENES, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PHAR, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

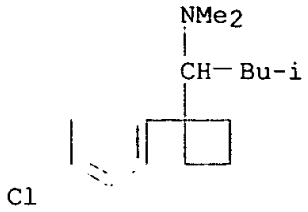


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

479 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
480 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d ide

L12 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 106650-56-0 REGISTRY
CN Cyclobutanemethanamine, 1-(4-chlorophenyl)-N,N-dimethyl-.alpha.-(2-methylpropyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Medaria
CN Meridia
CN Reductil
CN **Sibutramine**
FS 3D CONCORD
MF C17 H26 Cl N
CI COM
SR World Health Organization
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, DDFU, DIOGENES, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PHARMASEARCH, PIRA, PROMT, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

195 REFERENCES IN FILE CA (1967 TO DATE)
24 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
196 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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FILE COVERS 1907 - 22 Jul 2002  VOL 137 ISS 4
FILE LAST UPDATED: 21 Jul 2002  (20020721/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d que l64; d que l76; s l64 or l76

L51 (         4)SEA FILE=REGISTRY ABB=ON  PIOGLITAZONE?/CN
L52 (         7)SEA FILE=REGISTRY ABB=ON  TROGLITAZONE?/CN
L53 (         3)SEA FILE=REGISTRY ABB=ON  ROSIGLITAZONE?/CN
L54 (         1)SEA FILE=REGISTRY ABB=ON  INSULIN/CN
L55 (       526)SEA FILE=CAPLUS ABB=ON  L51 OR PIOGLITAZON# OR U72107
L56 (      1068)SEA FILE=CAPLUS ABB=ON  L52 OR TROGLITAZON# OR CI 991 OR CS
                045 OR GR 92132X OR ROMGLIZON#
L57 (       565)SEA FILE=CAPLUS ABB=ON  L53 OR ROSIGLITAZON# OR BRL 49653
L58 (    112158)SEA FILE=CAPLUS ABB=ON  L54 OR INSULIN/OBI
L59 (      1653)SEA FILE=CAPLUS ABB=ON  APPETITE DEPRESSANTS+OLD/CT
L60 (      1546)SEA FILE=CAPLUS ABB=ON  ANORECTIC#
L61 (       156)SEA FILE=CAPLUS ABB=ON  L58(L)(SENSITIZER# OR SENSITIZING(W)(
                AGENT# OR COMPOUND# OR DRUG#))/OBI
L62 (        11)SEA FILE=CAPLUS ABB=ON  ((L55 OR L56 OR L57) OR L61) AND (L59
                OR L60)
L63 (    297264)SEA FILE=CAPLUS ABB=ON  VISCOSITY
L64             8 SEA FILE=CAPLUS ABB=ON  L62 NOT L63



L65 (         4)SEA FILE=REGISTRY ABB=ON  PIOGLITAZONE?/CN
L66 (         7)SEA FILE=REGISTRY ABB=ON  TROGLITAZONE?/CN
L67 (         3)SEA FILE=REGISTRY ABB=ON  ROSIGLITAZONE?/CN
L68 (         3)SEA FILE=REGISTRY ABB=ON  MAZINDOL?/CN
L69 (         3)SEA FILE=REGISTRY ABB=ON  SIBUTRAMINE?/CN
L70 (       526)SEA FILE=CAPLUS ABB=ON  L65 OR PIOGLITAZON# OR U72107
L71 (      1068)SEA FILE=CAPLUS ABB=ON  L66 OR TROGLITAZON# OR CI 991 OR CS
                045 OR GR 92132X OR ROMGLIZON#
L72 (       565)SEA FILE=CAPLUS ABB=ON  L67 OR ROSIGLITAZON# OR BRL 49653
L73 (      6424)SEA FILE=CAPLUS ABB=ON  L68 OR MAZINDOL# OR AN 448 OR SAH
                42548
L74 (       219)SEA FILE=CAPLUS ABB=ON  L69 OR SIBATRAMIN#
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L75 (        19)SEA FILE=CAPLUS ABB=ON  ((L70 OR L71 OR L72)) AND (L73 OR L74)

L76           5 SEA FILE=CAPLUS ABB=ON  L75 AND (DIABET? OR COMBINATION)/TI



L145         11 L64 OR L76

=> fil wpids; d que l98; d que l102

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MOST RECENT DERWENT UPDATE            200245   <200245/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been
    enabled in WPINDEX/WPIDS and WPIX  >>>

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    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

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    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

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    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<


L88 (      2566)SEA FILE=WPIDS ABB=ON  ANORECTIC#
L89 (       127)SEA FILE=WPIDS ABB=ON  TROGLITAZON# OR CI 991 OR CS 045 OR GR
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L90 (        85)SEA FILE=WPIDS ABB=ON  ROSIGLITAZON# OR BRL 49653
L91 (        94)SEA FILE=WPIDS ABB=ON  PIOGLITAZON# OR U 72107
L92 (       391)SEA FILE=WPIDS ABB=ON  MAZINDOL# OR AN 448 OR SAH 42548
L93 (        76)SEA FILE=WPIDS ABB=ON  SIBUTRAMIN#
L94 (       289)SEA FILE=WPIDS ABB=ON  INSULIN(3A)SENSITI?
L95 (       116)SEA FILE=WPIDS ABB=ON  GLYCOS?(3A)(HAEMOGLOBIN# OR HEMOGLOBIN#)

L96 (        96)SEA FILE=WPIDS ABB=ON  ((L89 OR L90 OR L91) OR L94) AND (L92
                OR L88 OR L93)
L97 (        68)SEA FILE=WPIDS ABB=ON  HBA1C
L98           2 SEA FILE=WPIDS ABB=ON  L96 AND (L95 OR L97)



L99 (      2566)SEA FILE=WPIDS ABB=ON  ANORECTIC#
L100(        68)SEA FILE=WPIDS ABB=ON  INSULIN(W)(SENSITI!ER OR SENSITI!ING(W)(
                AGENT# OR COMPOUND# OR DRUG#))
L101(    431154)SEA FILE=WPIDS ABB=ON  COMBIN? OR SYNERG?
L102          5 SEA FILE=WPIDS ABB=ON  L99(L)L100(L)L101


=> s l98 or l102

L146          5 L98 OR L102

=> fil drugu; d que l110; d que l125; d que l142
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>>>  SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001.  <<<
>>>  (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION     <<<
>>>  SEE HELP COST                                        <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<


L108(      5744)SEA FILE=DRUGU ABB=ON  ANORECTIC/CT OR ANORECTICS/CT
L109(       154)SEA FILE=DRUGU ABB=ON  INSULIN(W)(SENSITI!ER OR SENSITI!ING(W)(
                AGENT# OR COMPOUND# OR DRUG#))
L110           4 SEA FILE=DRUGU ABB=ON  L108 AND L109



L111(          4)SEA FILE=REGISTRY ABB=ON  PIOGLITAZONE?/CN
L112(          7)SEA FILE=REGISTRY ABB=ON  TROGLITAZONE?/CN
L113(          3)SEA FILE=REGISTRY ABB=ON  ROSIGLITAZONE?/CN
L114(          3)SEA FILE=REGISTRY ABB=ON  MAZINDOL?/CN
L115(          3)SEA FILE=REGISTRY ABB=ON  SIBUTRAMINE?/CN
L116(        540)SEA FILE=DRUGU ABB=ON  L111 OR PIOGLITAZON# OR U72107
L117(        609)SEA FILE=DRUGU ABB=ON  L113 OR ROSIGLITAZON# OR BRL 49653
L118(       1229)SEA FILE=DRUGU ABB=ON  L112 OR TROGLITAZON# OR CI 991 OR CS
                045 OR GR 92132X OR ROMGLIZON#
L119(       1073)SEA FILE=DRUGU ABB=ON  L114 OR MAZINDOL# OR AN 448 OR SAH
                42548
L120(        117)SEA FILE=DRUGU ABB=ON  L115 OR SIBATRAMIN#
L121(        195)SEA FILE=DRUGU ABB=ON  SIBUTRAMINE/CT OR L120
L122(       5744)SEA FILE=DRUGU ABB=ON  ANORECTIC/CT OR ANORECTICS/CT
L123(       2501)SEA FILE=DRUGU ABB=ON  GLYCOS?(3A)(HAEMOGLOBIN# OR HEMOGLOBIN#)
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L124(       1302)SEA FILE=DRUGU ABB=ON  GLYCOSYLATED/CT AND HEMOGLOBIN/CT
L125           4 SEA FILE=DRUGU ABB=ON  L122 AND (L123 OR L124) AND (L116 OR
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L129(          3)SEA FILE=REGISTRY ABB=ON  MAZINDOL?/CN
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L131(        540)SEA FILE=DRUGU ABB=ON  L126 OR PIOGLITAZON# OR U72107
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L133(       1229)SEA FILE=DRUGU ABB=ON  L127 OR TROGLITAZON# OR CI 991 OR CS
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L134(       1073)SEA FILE=DRUGU ABB=ON  L129 OR MAZINDOL# OR AN 448 OR SAH
                42548
L135(        117)SEA FILE=DRUGU ABB=ON  L130 OR SIBATRAMIN#
L136(        195)SEA FILE=DRUGU ABB=ON  SIBUTRAMINE/CT OR L135
L137(       5744)SEA FILE=DRUGU ABB=ON  ANORECTIC/CT OR ANORECTICS/CT
L138(        154)SEA FILE=DRUGU ABB=ON  INSULIN(W)(SENSITI!ER OR SENSITI!ING(W)(
                AGENT# OR COMPOUND# OR DRUG#))
L139(         33)SEA FILE=DRUGU ABB=ON  ((L131 OR L132 OR L133) OR L138) AND
                (L134 OR L135 OR L136 OR L137)
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L141(     24350)SEA FILE=DRUGU ABB=ON  12/CC - concept code - antidiabetics
L142          7 SEA FILE=DRUGU ABB=ON  L140 AND L139 AND L141


=> s l110 or l125 or l142

L147         14 L110 OR L125 OR L142

=> fil medl

FILE 'MEDLINE' ENTERED AT 17:14:41 ON 22 JUL 2002

 FILE LAST UPDATED: 20 JUL 2002 (20020720/UP). FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> d que l13; d que l15; s l13 or l15

L1          2498 SEA FILE=MEDLINE ABB=ON  APPETITE DEPRESSANTS/CT
L2           369 SEA FILE=MEDLINE ABB=ON  INSULIN(W)(SENSITI!ER# OR SENSITI!ING(
                 W)(DRUG# OR AGENT# OR COMPOUND#))
L6          1009 SEA FILE=MEDLINE ABB=ON  TROGLITAZON# OR CI 991 OR CS 045 OR
                 GR 92132# OR ROMGLIZON#
L7           448 SEA FILE=MEDLINE ABB=ON  ROSIGLITAZON# OR BRL 49653
L8           385 SEA FILE=MEDLINE ABB=ON  PIOGLITAZON# OR U 72107
L9          3754 SEA FILE=MEDLINE ABB=ON  MAZINDOL# OR AN 448 OR SAH 42548
L10          251 SEA FILE=MEDLINE ABB=ON  SIBUTRAMIN#
L13            4 SEA FILE=MEDLINE ABB=ON  (L2 OR L6 OR L7 OR L8) AND (L1 OR L9
                 OR L10)



L1          2498 SEA FILE=MEDLINE ABB=ON  APPETITE DEPRESSANTS/CT
L2           369 SEA FILE=MEDLINE ABB=ON  INSULIN(W)(SENSITI!ER# OR SENSITI!ING(
                 W)(DRUG# OR AGENT# OR COMPOUND#))
L3          8046 SEA FILE=MEDLINE ABB=ON  HEMOGLOBIN A, GLYCOSYLATED/CT
L6          1009 SEA FILE=MEDLINE ABB=ON  TROGLITAZON# OR CI 991 OR CS 045 OR
                 GR 92132# OR ROMGLIZON#
L7           448 SEA FILE=MEDLINE ABB=ON  ROSIGLITAZON# OR BRL 49653
L8           385 SEA FILE=MEDLINE ABB=ON  PIOGLITAZON# OR U 72107
L9          3754 SEA FILE=MEDLINE ABB=ON  MAZINDOL# OR AN 448 OR SAH 42548
L10          251 SEA FILE=MEDLINE ABB=ON  SIBUTRAMIN#
L14          130 SEA FILE=MEDLINE ABB=ON  L3(L)DE/CT - Subheading DE - drug effects
L15           10 SEA FILE=MEDLINE ABB=ON  L14 AND (L1 OR L2 OR (L6 OR L7 OR L8
                 OR L9 OR L10))



L148         14 L13 OR L15

=> fil embase; d que l39

FILE 'EMBASE' ENTERED AT 17:14:43 ON 22 JUL 2002
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 FILE COVERS 1974 TO 18 Jul 2002 (20020718/ED)
```

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L29         1217 SEA FILE=EMBASE ABB=ON  ANOREXIGENIC AGENT/CT
L30          372 SEA FILE=EMBASE ABB=ON  INSULIN(W)(SENSITI!ER# OR SENSITI!ING(W
                 )(DRUG# OR AGENT# OR COMPOUND#))
L31         1710 SEA FILE=EMBASE ABB=ON  TROGLITAZONE/CT
L32          816 SEA FILE=EMBASE ABB=ON  ROSIGLITAZONE/CT
L33          787 SEA FILE=EMBASE ABB=ON  PIOGLITAZONE/CT
L34         1284 SEA FILE=EMBASE ABB=ON  MAZINDOL/CT
L35          544 SEA FILE=EMBASE ABB=ON  SIBUTRAMINE/CT
L36         4020 SEA FILE=EMBASE ABB=ON  GLYCOSYLATED HEMOGLOBIN/CT OR GLYCOSYLA
                 TED HEMOGLOBIN A 1/CT OR GLYCOSYLATED HEMOGLOBIN A1C/CT
L39            2 SEA FILE=EMBASE ABB=ON  (L29 OR L34 OR L35) AND ((L30 OR L31
                 OR L32 OR L33)) AND L36


=> dup rem l148,l147,l145,l139,l146
FILE 'MEDLINE' ENTERED AT 17:15:16 ON 22 JUL 2002

FILE 'DRUGU' ENTERED AT 17:15:16 ON 22 JUL 2002
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FILE 'CAPLUS' ENTERED AT 17:15:16 ON 22 JUL 2002
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FILE 'WPIDS' ENTERED AT 17:15:16 ON 22 JUL 2002
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PROCESSING COMPLETED FOR L148
PROCESSING COMPLETED FOR L147
PROCESSING COMPLETED FOR L145
PROCESSING COMPLETED FOR L39
PROCESSING COMPLETED FOR L146
L149           45 DUP REM L148 L147 L145 L39 L146 (1 DUPLICATE REMOVED)
                  ANSWERS '1-14' FROM FILE MEDLINE
                  ANSWERS '15-28' FROM FILE DRUGU
                  ANSWERS '29-39' FROM FILE CAPLUS
                  ANSWERS '40-41' FROM FILE EMBASE
                  ANSWERS '42-45' FROM FILE WPIDS

=> d ibib ab hitrn 1-45

L149 ANSWER 1 OF 45     MEDLINE
ACCESSION NUMBER:    2002149050     MEDLINE
DOCUMENT NUMBER:     21873560   PubMed ID: 11881246
TITLE:               [A case report. Rosiglitazone treatment was
                     highly effective yet had to be terminated].
                     Fallbeskrivning. Rosiglitazonbehandling gav kraftfull
                     effekt, men fick anda avbrytas.
AUTHOR:              Ridderstrale Martin; Groop Leif
CORPORATE SOURCE:    Endokrinologiska kliniken, Universitetssjukhuset MAS,
                     Malmo.. martin.ridderstrale@endo.mas.lu.se
SOURCE:              LAKARTIDNINGEN, (2002 Jan 31) 99 (5) 407-10.
                     Journal code: 0027707. ISSN: 0023-7205.
```

PUB. COUNTRY: Sweden
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Swedish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020308
Last Updated on STN: 20020410
Entered Medline: 20020409

AB The thiazolidinediones were introduced as oral hypoglycemic drugs in Sweden during the fall of 2000. A case is reported in which a woman with insulin-dependent type-2 diabetes and both macro- and microangiopathy and pronounced insulin resistance was treated with **rosiglitazone** (Avandia). Within three months insulin doses could be reduced by 36% (from 176 to 112 units insulin daily) and concomitantly Ery-HbA1c was reduced from 8.4 to 5.3%. In spite of this dramatic effect on glucose homeostasis administration of the drug had to be discontinued due to critical congestive heart failure.

L149 ANSWER 2 OF 45 MEDLINE
ACCESSION NUMBER: 2001531677 MEDLINE
DOCUMENT NUMBER: 21461543 PubMed ID: 11577798
TITLE: Repaglinide: a review of its therapeutic use in type 2 diabetes mellitus.
AUTHOR: Culy C R; Jarvis B
CORPORATE SOURCE: Adis International Limited, Mairangi Bay, Auckland, New Zealand.. demail@adis.co.nz
SOURCE: DRUGS, (2001) 61 (11) 1625-60. Ref: 113
Journal code: 7600076. ISSN: 0012-6667.
PUB. COUNTRY: New Zealand
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20011002
Last Updated on STN: 20020206
Entered Medline: 20020205

AB Repaglinide, a carbamoylmethyl benzoic acid derivative, is the first of a new class of oral antidiabetic agents designed to normalise postprandial glucose excursions in patients with type 2 diabetes mellitus. Like the sulphonylureas, repaglinide reduces blood glucose by stimulating insulin release from pancreatic beta-cells, but differs from these and other antidiabetic agents in its structure, binding profile, duration of action and mode of excretion. In clinical trials of up to 1-year's duration, repaglinide maintained or improved glycaemic control in patients with type 2 diabetes mellitus. In comparative, 1-year, double-blind, randomised trials (n = 256 to 544), patients receiving repaglinide (0.5 to 4mg before 3 daily meals) achieved similar glycaemic control to that in patients receiving glibenclamide (glyburide) < or = 15 mg/day and greater control than patients receiving glipizide < or = 15 mg/day. Changes from baseline in glycosylated haemoglobin and fasting blood glucose levels were similar between patients receiving repaglinide and glibenclamide in all studies; however, repaglinide was slightly better than glibenclamide in reducing postprandial blood glucose in I short term study (n = 192). Patients can vary their meal timetable with repaglinide: the glucose-lowering efficacy of repaglinide was similar for patients consuming 2, 3 or 4 meals a day. Repaglinide showed additive effects when used in combination with other oral antidiabetic agents including metformin, **troglitazone**, **rosiglitazone** and **pioglitazone**, and intermediate-acting insulin (NPH) given at bedtime. In 1-year trials, the most common adverse events reported in repaglinide recipients (n = 1,228) were hypoglycaemia (16%), upper respiratory tract infection (10%), rhinitis (7%), bronchitis

(6%) and headache (9%). The overall incidence of hypoglycaemia was similar to that recorded in patients receiving glibenclamide, glipizide or gliclazide (n = 597) [18%]; however, the incidence of serious hypoglycaemia appears to be slightly higher in sulphonylurea recipients. Unlike glibenclamide, the risk of hypoglycaemia in patients receiving repaglinide was not increased when a meal was missed in 1 trial. In conclusion, repaglinide is a useful addition to the other currently available treatments for type 2 diabetes mellitus. Preprandial repaglinide has displayed antihyperglycaemic efficacy at least equal to that of various sulphonylureas and is associated with a reduced risk of serious hypoglycaemia. It is well tolerated in a wide range of patients, including the elderly, even if a meal is missed. Furthermore, glycaemic control is improved when repaglinide is used in combination with metformin. Thus, repaglinide should be considered for use in any patient with type 2 diabetes mellitus whose blood glucose cannot be controlled by diet or exercise alone, or as an adjunct in patients whose glucose levels are inadequately controlled on metformin alone.

L149 ANSWER 3 OF 45 MEDLINE
ACCESSION NUMBER: 2001482005 MEDLINE
DOCUMENT NUMBER: 21416794 PubMed ID: 11525086
TITLE: [The thiazolidinedione derivates: a new class of oral blood glucose lowering agents].
De thiazolidinedionderivaten: een nieuwe klasse orale bloedglucoseverlagende middelen.
COMMENT: Comment in: Ned Tijdschr Geneeskd. 2001 Sep 29;145(39):1911-2
AUTHOR: Jazet I M; Meinders A E
CORPORATE SOURCE: Leids Universitair Medisch Centrum, afd. Algemene Interne Geneeskunde, Albinusdreef 2, 2333 ZA Leiden..
i.m.jazet@lumc.nl
SOURCE: NEDERLANDS TIJDSCHRIFT VOOR GENEESKUNDE, (2001 Aug 11) 145 (32) 1541-7. Ref: 39
Journal code: 0400770. ISSN: 0028-2162.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Dutch
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010830
Last Updated on STN: 20020424
Entered Medline: 20011004

AB The thiazolidine-dione derivatives are a new class of oral blood-glucose lowering drugs in type 2 diabetes. They increase the sensitivity of target tissues to insulin, thereby reducing insulin resistance. They act by activation of a specific nuclear receptor--the peroxisome proliferator-activated receptor gamma (PPAR-gamma)--which increases transcription of certain genes involved in adipocyte differentiation and lipid and glucose metabolism. They increase glucose disposal, reduce hepatic glucose output and reduce both plasma glucose and circulating insulin. By reducing insulin requirements the hypersecretion of the beta cell can be diminished, thereby sparing beta cell function. Thiazolidine-dione derivatives reduce plasma glycosylated haemoglobin (HbA1c) by about 1 to 2%. Combination therapy with sulphonylurea derivatives or metformin seems to be more effective, i.e. lower dosages of either agent or both are sufficient to achieve the same reduction in plasma glucose and HbA1c as monotherapy. The thiazolidine-dione derivatives are generally well tolerated and the new drugs such as **rosiglitazone** and **pioglitazone** do not seem to be associated with idiosyncratic hepatotoxicity.

L149 ANSWER 4 OF 45 MEDLINE
ACCESSION NUMBER: 2002012942 MEDLINE
DOCUMENT NUMBER: 21300379 PubMed ID: 11407727
TITLE: Beneficial effect of **troglitazone**, an insulin-sensitizing antidiabetic agent, on coronary circulation in patients with non-insulin-dependent diabetes mellitus.
AUTHOR: Sekiya M; Suzuki J; Watanabe K; Funada J; Otani T; Akutsu H
CORPORATE SOURCE: Department of Cardiology, Ehime National Hospital, Onsen-gun, Japan.. msekiya@ehime-nh.go.jp
SOURCE: JAPANESE CIRCULATION JOURNAL, (2001 Jun) 65 (6) 487-90. Journal code: 7806868. ISSN: 0047-1828.
PUB. COUNTRY: Australia
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020208
Entered Medline: 20020207

AB Evidence is increasing for small vessel remodeling and disturbance of endothelium-dependent vasodilation in diabetic patients. Insulin increases vascular wall thickening and produces endothelial dysfunction. **Troglitazone**, a new **insulin-sensitizer** antidiabetic agent, is considered to reduce plasma insulin level and the present study assessed its effect on the coronary circulation of the patients with non-insulin-dependent diabetes mellitus (NIDDM). Analysis of the myocardial washout rate with adenosine triphosphate-stress thallium-201 scintigraphy was used to estimate coronary circulation, and for estimation of insulin sensitivity, the homeostasis model insulin resistance index (HOMA-R) was calculated. Patients were treated with monotherapy of either **troglitazone** (200 mg bid, n=12) or glibenclamide (2.5 mg daily, n=12) for 3 months. Age-, sex- and risk factors-matched subjects without NIDDM were employed as a control. Fasting plasma glucose and hemoglobin A1c were similarly decreased by **troglitazone** or glibenclamide. Plasma insulin level (pmol/L) decreased from 66.6+/-10.8 to 39.0+/-7.2 with **troglitazone**, but was unchanged by glibenclamide (58.8+/-7.2 to 66.0+/-10.8). The diabetic groups had a significantly lower washout rate than controls, which was improved by **troglitazone**, but not by glibenclamide. In addition, the increase in washout rate correlated significantly with the decrease in HOMA-R in the **troglitazone** group. In conclusion, **troglitazone** can restore coronary circulation by improving insulin resistance in patients with NIDDM.

L149 ANSWER 5 OF 45 MEDLINE
ACCESSION NUMBER: 2001445046 MEDLINE
DOCUMENT NUMBER: 21383272 PubMed ID: 11491207
TITLE: The impact of **pioglitazone** on glycemic control and atherogenic dyslipidemia in patients with type 2 diabetes mellitus.
AUTHOR: Rosenblatt S; Miskin B; Glazer N B; Prince M J; Robertson K E
CORPORATE SOURCE: Irvine Clinical Research Center, California, USA. (Pioglitazone 026 Study Group).
SOURCE: CORONARY ARTERY DISEASE, (2001 Aug) 12 (5) 413-23. Journal code: 9011445. ISSN: 0954-6928.
PUB. COUNTRY: England: United Kingdom
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)

(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20020121
Entered Medline: 20011207

AB BACKGROUND: To evaluate the glycemic control, lipid effects, and safety of **pioglitazone** in patients with type 2 diabetes mellitus. DESIGN AND METHODS: Patients (n = 197) with type 2 diabetes mellitus, a hemoglobin A1c (HbA1c) > or = 8.0%, fasting plasma glucose (FPG) > 7.7 mmol/l (140 mg/dl), and C-peptide > 0.331 nmol/l (1 ng/ml) were enrolled in this 23-week multi-center (27 sites), double-blind clinical trial and randomized to receive either a placebo or **pioglitazone** HCl 30 mg (**pioglitazone**), administered once daily, as monotherapy. Patients were required to discontinue all anti-diabetic medications 6 weeks before receiving study treatment. Efficacy parameters included HbA1c fasting plasma glucose (FPG), serum C-peptide, insulin, triglycerides (Tg), and cholesterol (total cholesterol [TC], high-density lipoprotein-cholesterol [HDL-C], low-density lipoprotein-cholesterol [LDL-C]). Adverse event rates, serum chemistry, and physical examinations were recorded. RESULTS: Compared with placebo, **pioglitazone** significantly (P= 0.0001) reduced HbA1c (-1.37% points), FPG (-3.19 mmol/l; -57.5 mg/dl), fasting C-peptide (-0.076+/-0.022 nmol/l), and fasting insulin (-11.88+/-4.70 pmol/l). **Pioglitazone** significantly (P < 0.001) decreased insulin resistance (HOMA-IR; -12.4+/-7.46%) and improved beta-cell function (Homeostasis Model Assessment (HOMA-BCF); +47.7+/-11.58%). Compared with placebo, fasting serum Tg concentrations decreased (-16.6%; P = 0.0178) and HDL-C concentrations increased (+12.6%; P= 0.0065) with **pioglitazone** as monotherapy. Total cholesterol and LDL-C changes were not different from placebo. The overall adverse event profile of **pioglitazone** was similar to that of placebo, with no evidence of drug-induced elevations of serum alanine transaminase (ALT) concentrations or hepatotoxicity. CONCLUSIONS: **Pioglitazone** improved insulin resistance and glycemic control, as well as Tg and HDL-C - which suggests that **pioglitazone** may reduce cardiovascular risk for patients with type 2 diabetes.

L149 ANSWER 6 OF 45 MEDLINE
ACCESSION NUMBER: 2001432921 MEDLINE
DOCUMENT NUMBER: 21373478 PubMed ID: 11480129
TITLE: Actos (**pioglitazone**): a new treatment for type 2 diabetes.
AUTHOR: Lawrence J M; Reckless J P
CORPORATE SOURCE: Diabetes and Lipid Research, Royal United Hospital, Bath BA1 3NG.
SOURCE: HOSPITAL MEDICINE, (2001 Jul) 62 (7) 411-6. Ref: 20
Journal code: 9803882. ISSN: 1462-3935.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010903
Last Updated on STN: 20010903
Entered Medline: 20010830

AB Type 2 diabetes is increasingly common and can be difficult to control. By directly targeting insulin resistance, the thiazolidinediones offer a new mode of treatment. Here, the pharmacology, clinical trial evidence, side-effects and current clinical uses of **pioglitazone** are

reviewed.

L149 ANSWER 7 OF 45 MEDLINE
ACCESSION NUMBER: 2002182534 MEDLINE
DOCUMENT NUMBER: 21912900 PubMed ID: 11916103
TITLE: The importance of obesity in diabetes and its treatment with **sibutramine**.
AUTHOR: Van Gaal L F; Peiffer F W
CORPORATE SOURCE: Department of Diabetology, Metabolism and Clinical Nutrition, Faculty of Medicine, University Hospital Antwerp, Belgium.. luc.van.gaal@uza.be
SOURCE: INTERNATIONAL JOURNAL OF OBESITY AND RELATED METABOLIC DISORDERS, (2001 Dec) 25 Suppl 4 S24-8. Ref: 19
Journal code: 9313169. ISSN: 0307-0565.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020403
Last Updated on STN: 20020614
Entered Medline: 20020522

AB Weight gain is a known risk factor for the development of type 2 diabetes and even modest weight reduction can reduce the risk of developing diabetes, so controlling body weight is an important public health goal in the fight against diabetes and its comorbidities. Weight reduction is also a cornerstone of diabetes management, improving glycaemic control and reducing other risk factors associated with this disease. Pharmacotherapies such as **sibutramine** contribute to the management of type 2 diabetes in overweight and obese patients.

L149 ANSWER 8 OF 45 MEDLINE
ACCESSION NUMBER: 2002181091 MEDLINE
DOCUMENT NUMBER: 21910930 PubMed ID: 11912814
TITLE: Treatment strategies and new therapeutic advances for type 2 diabetes.
AUTHOR: Rosenstock J
SOURCE: DIABETES EDUCATOR, (2000 Nov-Dec) 26 Suppl 14-8.
Journal code: 7701401. ISSN: 0145-7217.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Nursing Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020401
Last Updated on STN: 20020423
Entered Medline: 20020422

AB Because type 2 diabetes is caused by two defects, impaired insulin secretion and insulin resistance, logical management of diabetes will include combination therapies to treat this dual condition. Initial combination therapy should include an insulin secretagogue and an **insulin sensitizer**, with the addition of insulin in the evening if the HbA1c remains greater than 8%. Treatment to target should be clearly defined to achieve HbA1c < 7% unless there are specific individual considerations that make higher HbA1c levels acceptable or desirable. Patients are now treated earlier, when fasting blood glucose levels are in the 126 to 140 mg/dL range; and drugs with less chances of hypoglycemia are preferred at this stage. However, low-dose combination therapy as an early initial treatment, if HbA1c remains > 7%, is an emerging aggressive strategy that requires further consideration and further studies to prove its long-term efficacy and safety.

L149 ANSWER 9 OF 45 MEDLINE
ACCESSION NUMBER: 2000222506 MEDLINE
DOCUMENT NUMBER: 20222506 PubMed ID: 10761869
TITLE: New agents for Type 2 diabetes.
AUTHOR: Nattrass M; Bailey C J
CORPORATE SOURCE: Diabetes Resource Centre, Selly Oak Hospital, Birmingham, UK.
SOURCE: BAILLIERES BEST PRACTICE & RESEARCH. CLINICAL ENDOCRINOLOGY & METABOLISM, (1999 Jul) 13 (2) 309-29. Ref: 73
Journal code: 100957144. ISSN: 1521-690X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000613
Last Updated on STN: 20000824
Entered Medline: 20000531

AB Current agents for the treatment of Type 2 diabetes mellitus improve the metabolic profile but do not reinstate normality. They also reduce chronic diabetic complications, but they do not eliminate them. Thus, new agents with novel actions are required to complement and extend the capabilities of existing treatments. Insulin resistance and beta-cell failure, which are crucial components in the pathogenesis of Type 2 diabetes, remain the underlying targets for new drugs. Recently introduced agents include a short-acting non-sulphonylurea insulin-releaser, repaglinide, which synchronizes insulin secretion with meal digestion in order to reduce post-prandial hyperglycaemia. The thiazolidinedione drugs, **troglitazone**, **rosiglitazone** and **pioglitazone** represent a new class of agonists for the nuclear receptor peroxisome proliferator-activated receptor-gamma (PPARgamma). PPARgamma increases the transcription of certain insulin-sensitive genes, thereby improving insulin sensitivity. The intestinal lipase inhibitor orlistat and the satiety-inducer **sibutramine** are new weight-reducing agents that may benefit glycaemic control in obese Type 2 diabetes patients. Several further new insulin-releasing agents, and agents to retard carbohydrate digestion and modify lipid metabolism stand poised to enter the market. The extent to which they will benefit glycaemic control remains to be seen. However, the prospect of permanently arresting or reversing the progressive deterioration of Type 2 diabetes continues to evade therapeutic capture.

L149 ANSWER 10 OF 45 MEDLINE
ACCESSION NUMBER: 2000071653 MEDLINE
DOCUMENT NUMBER: 20071653 PubMed ID: 10603986
TITLE: **Rosiglitazone** for type 2 diabetes mellitus.
AUTHOR: Anonymous
SOURCE: MEDICAL LETTER ON DRUGS AND THERAPEUTICS, (1999 Aug 13) 41 (1059) 71-3.
Journal code: 2985240R. ISSN: 0025-732X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991227

L149 ANSWER 11 OF 45 MEDLINE

ACCESSION NUMBER: 2001150891 MEDLINE
DOCUMENT NUMBER: 21114709 PubMed ID: 11220287
TITLE: Promising new approaches.
AUTHOR: Reasner C A 2nd
CORPORATE SOURCE: Texas Diabetes Institute, University of Texas Health Science Center, San Antonio 78229-4493, USA..
tjbarries@university-health-sys.com
SOURCE: DIABETES, OBESITY & METABOLISM, (1999 May) 1 Suppl 1 S41-8.
Ref: 35
Journal code: 100883645. ISSN: 1462-8902.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010315

AB Insulin resistance in liver and muscle tissue, together with beta-cell secretory defects, leads to overt type 2 diabetes mellitus. In the early stages of this progressive disorder, glycaemic control can be established through diet and exercise alone. Indeed, in some patients, marked weight reduction can lead to normalized fasting blood glucose. As a consequence, pharmacological approaches to weight loss have been investigated as a new option for the management of type 2 diabetes in obese patients. The serotonin- and noradrenaline-reuptake inhibitor **sibutramine** has emerged as the most promising agent in the treatment of obesity, although it appears to be less effective in diabetic patients than in non-diabetic patients. Other weight-reducing agents of potential benefit include noradrenergic anorexiants, orlistat, leptin, and beta3-agonists. Insulin and insulin secretagogues, the oldest available antidiabetic drugs, have been used to compensate for beta-cell secretory defects in patients with type 2 diabetes. Repaglinide, a new, fast-acting insulin secretagogue with a short duration of action, reduces postprandial hyperglycaemia when taken shortly before meals. Other novel antidiabetic agents are currently under development, including pramlintide (an amylin analogue) and glucagon-like peptide. Pramlintide slows gastric emptying and delays glucose absorption, and glucagon-like peptide is the most potent endogenous stimulator of glucose-induced insulin release. Recent advances in type 2 diabetes therapy have seen the development of the thiazolidinediones (**troglitazone**, **rosiglitazone**, and **pioglitazone**), which improve insulin resistance in patients whose diabetes is poorly controlled by diet and exercise therapy. Thiazolidinediones bind to peroxisome proliferator-activated receptor-gamma (PPAR-gamma) and act through a process involving gene regulation at a transcriptional level. **Troglitazone**, the first approved drug in the class, has been shown to decrease plasma glucose levels as monotherapy but is more effective in combination with sulphonylureas, metformin, or insulin. However, despite its generally good safety profile, **troglitazone** has been associated with severe idiosyncratic hepatocellular injury. There have been more than 150 spontaneous reports of serious hepatic events, including at least 25 instances in which patients died or required a liver transplant. **Rosiglitazone**, the most potent thiazolidinedione, is still in clinical development, as is **pioglitazone**. To date, **rosiglitazone** has been shown to have no reported cases of idiosyncratic drug reactions leading to jaundice or liver failure and no clinically significant drug interactions with cytochrome P450 3A4-metabolized drugs such as nifedipine. Although the available data for **pioglitazone** are limited to the results of short-term studies, it is reported to be safe and well tolerated. Combination therapy is increasingly important in type 2 diabetes management following failure of

monotherapy because complementary mechanisms of action of the different classes of oral agents demonstrate synergistic effects when used in combination. Oral agents may also be used as adjuncts to insulin for achieving glycaemic control.

L149 ANSWER 12 OF 45 MEDLINE
ACCESSION NUMBER: 1999229309 MEDLINE
DOCUMENT NUMBER: 99229309 PubMed ID: 10212839
TITLE: Insulin resistance: site of the primary defect or how the current and the emerging therapies work.
AUTHOR: Kolaczynski J W; Caro J F
CORPORATE SOURCE: Eli Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285, USA.
SOURCE: JOURNAL OF BASIC AND CLINICAL PHYSIOLOGY AND PHARMACOLOGY, (1998) 9 (2-4) 281-94. Ref: 63
Journal code: 9101750. ISSN: 0792-6855.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990714
Last Updated on STN: 19990714
Entered Medline: 19990630

AB Insulin resistance is one of the cardinal pathophysiological components of the metabolic syndrome, type 2 diabetes, and frequently co-exists with essential hypertension. Although insulin resistance is defined as inadequate target organ (muscle, liver and fat) responsiveness and/or sensitivity to insulin, the primary defect may be located in the target organs themselves or at their remote controller--the central nervous system. One of the ways of resolving this dilemma is studying the mechanisms of action of drugs that have insulin-sensitizing properties. In this brief review we discuss how the known and potential **insulin sensitizers**: metformin, appetite suppressants, thiazolidinediones, and the new class of centrally acting antihypertensive drugs, Il-receptor agonists, may work.

L149 ANSWER 13 OF 45 MEDLINE
ACCESSION NUMBER: 1998047328 MEDLINE
DOCUMENT NUMBER: 98047328 PubMed ID: 9388135
TITLE: From the Food and Drug Administration.
AUTHOR: Nightingale S L
SOURCE: JAMA, (1997 Dec 3) 278 (21) 1728.
Journal code: 7501160. ISSN: 0098-7484.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971211

L149 ANSWER 14 OF 45 MEDLINE
ACCESSION NUMBER: 96375455 MEDLINE
DOCUMENT NUMBER: 96375455 PubMed ID: 8781766
TITLE: **Troglitazone**, an insulin action enhancer, improves metabolic control in NIDDM patients. **Troglitazone** Study Group.
COMMENT: Erratum in: Diabetologia 1996 Oct;39(10):1245
AUTHOR: Kumar S; Boulton A J; Beck-Nielsen H; Berthezene F; Muggeo

M; Persson B; Spinas G A; Donoghue S; Lettis S; Stewart-Long P
CORPORATE SOURCE: Department of Medicine, Manchester Royal Infirmary, UK.
SOURCE: DIABETOLOGIA, (1996 Jun) 39 (6) 701-9.
Journal code: 0006777. ISSN: 0012-186X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19980206
Entered Medline: 19961205

AB The effects of **troglitazone**, a novel thiazolidinedione, in non-insulin-dependent diabetic (NIDDM) patients were studied in a double-blind, parallel-group, placebo-controlled, dose-ranging trial. A total of 330 patients (63% male), mean age 57 years (range 39-72), with two fasting capillary blood glucose values > or = 7 and < or = 15 mmol/l (within 2.5 mmol/l of each other) were randomised to treatment with placebo or **troglitazone** at doses of 200, 400, 600 or 800 mg once daily, or 200 or 400 mg twice daily, for 12 weeks. Prior to the study, treatment had been with diet alone (38% patients) or with oral hypoglycaemic agents which were stopped 3-4 weeks before study treatment started. During treatment, HbA1c tended to rise in patients taking placebo (7.2-8.0%), but remained unchanged with all doses of **troglitazone** . After 12 weeks of treatment, HbA1c was significantly lower in the **troglitazone**-treated (mean 7.0-7.4%) compared to the placebo-treated (8.0%) patients (p = 0.055 to < 0.001), as was fasting serum glucose concentration (**troglitazone**, 9.3-11.0 mmol/l vs placebo, 12.9 mmol/l, p < 0.001). All doses of **troglitazone** were equally effective. **Troglitazone** also lowered fasting plasma insulin concentration, by 12-26% compared to placebo (p = 0.074 to < 0.001). Insulin sensitivity assessed by homeostasis model assessment (HOMA) was greater after 12 weeks of treatment in **troglitazone** -treated patients (**troglitazone**, 34.3-42.8% vs placebo, 29.9%, p < 0.05). In addition, serum triglyceride and non-esterified fatty acid concentrations were significantly lower and HDL cholesterol higher at **troglitazone** doses of 600 and 800 mg/day. LDL cholesterol increased at 400 and 600 mg doses only (from 4.3 and 3.9 mmol/l at baseline to 4.8 and 4.5 mmol/l, respectively at 12 weeks, p < 0.05), but not at doses of 800 mg once daily or 400 mg twice daily. LDL/HDL ratio did not change during treatment. All doses were well tolerated; incidence of adverse events in **troglitazone**-treated patients was no higher than in those treated with placebo. However, a tendency to reduced neutrophil counts was observed in patients taking the highest doses of **troglitazone**. We conclude that **troglitazone** is effective and well-tolerated and shows potential as a new therapeutic agent for the treatment of NIDDM.

L149 ANSWER 15 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-19351 DRUGU T E S
TITLE: Advances in endocrinology and metabolic medicine.
AUTHOR: Malik I A; Williams G
CORPORATE SOURCE: Univ.Liverpool
LOCATION: Liverpool, U.K.
SOURCE: Practitioner (246, No. 1633, 223-34, 2002) 2 Fig. 2 Tab. 15 Ref.
CODEN: PRACAK ISSN: 0192-6160
AVAIL. OF DOC.: Department of Diabetes and Endocrinology, University Hospital Aintree, Liverpool, England.

LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Advances in endocrinology and metabolic medicine are reviewed. The symptoms and clinical features of GH deficiency are tabulated. Therapeutic options in obesity such as orlistat, sibutramine and ghrelin are discussed. The role of GH replacement in adults and developments in glucose monitoring are considered. Pancreatic islet cell transplantation and **insulin-sensitizing agents** (**rosiglitazone** and **pioglitazone**) are also mentioned. The implications of the discovery of ghrelin include development of a ghrelin antagonist to treat obesity.

L149 ANSWER 16 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-10348 DRUGU T S
TITLE: The long-term outcomes of sibutramine effectiveness on weight (LOSE weight) study in a managed care organization: six month outcomes in a naturalistic clinical setting.
AUTHOR: Porter J A; Raebel M A; Lanty F A; Conner D A; Vogel E A; Gay E C; Nugent E W; Merenich J A
LOCATION: Littleton, Colo., USA
SOURCE: Circulation (104, No. 17, Suppl., 793, 2001) 1 Tab.
CODEN: CIRCAZ ISSN: 0009-7322
AVAIL. OF DOC.: Kaiser Permanente, Littleton, CO, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB This prospective, randomized study assesses the impact of sibutramine in combination with a weight management program in the naturalistic setting of Kaiser Permanente of Colorado. Preliminary safety data indicate sibutramine is well tolerated. A weight management program with drug therapy is significantly more effective at achieving weight loss than a weight management program alone. This study is the largest to date to evaluate the effectiveness of obesity drug therapy in a naturalistic setting and confirms the effectiveness of sibutramine seen in clinical trials. (conference abstract: Scientific Sessions of the American Heart Association, Anaheim, California, USA, 2001).

L149 ANSWER 17 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-05759 DRUGU T
TITLE: Sibutramin in normo- and hypertensive patients - new insights from a PMS-study.
AUTHOR: Scholze J
CORPORATE SOURCE: Univ.Berlin-Humboldt
LOCATION: Berlin, Ger.
SOURCE: Dtsch.Med.Wochenschr. (126, Suppl. 3, S198, 2001)
CODEN: DMWOAX ISSN: 0012-0472
AVAIL. OF DOC.: Outpatient Clinic of Internal Medicine, University Hospital Charite Berlin, Germany.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB A post marketing surveillance study (PMS) was conducted to investigate the efficacy and safety of sibutramine (SIB) under real life conditions in 6360 obese patients. SIB very effectively reduced not only body weight, but also the cardiovascular risk profile, particularly in overweight patients with high risk profiles at baseline. (conference abstract: 25th Scientific Meeting of the German League for Controlling High Blood Pressure, Bielefeld, Germany, 2001).

L149 ANSWER 18 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-35780 DRUGU T E
TITLE: Potential new treatments for type 2 diabetes.
AUTHOR: Bailey C J
CORPORATE SOURCE: Univ.Aston
LOCATION: Birmingham, U.K.
SOURCE: Trends Pharmacol.Sci. (21, No. 7, 259-65, 2000) 3 Fig. 1 Tab. 75 Ref.
CODEN: TPHSDY ISSN: 0165-6147
AVAIL. OF DOC.: School of Life and Health Sciences, Aston University, Birmingham, England B4 7ET. (e-mail: c.j.bailey@aston.ac.uk).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Potential new therapies for NIDDM are reviewed. The limitations of current drugs (sulfonylureas, repaglinide, metformin, alpha-glucosidase inhibitors, thiazolidinediones) and ways of improving insulin action (**troglitazone, rosiglitazone, pioglitazone,** darglitazone, T-174, MCC-555, DRF-2189, KRP-297, BM-152054, JTT-501, GW-1929, vanadium salts, LY-783281) are discussed. Treatment targets are cited. The actions of new insulin releasers (repaglinide, nateglinide, KAD-1229, glucagon-like peptide-1, L-686398, JTT-608, succinate esters), anti-obesity agents (orlistat, 5-HT, sibutramine, bromocriptine, pramlintide), dietary supplements, metabolic modulators, and insulin analogs (lispro, aspart) are explained. There is a need for new antidiabetic agents as current therapies are unable to control hyperglycemia or to reinstate near-normal metabolic homeostasis.

L149 ANSWER 19 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-34189 DRUGU T E
TITLE: Diabetes mellitus. New drugs for diabetics.
AUTHOR: Menzel R
LOCATION: Greifswald, Ger.
SOURCE: Dtsch.Apoth.Ztg. (139, No. 30, 2883-86, 1999) 2 Fig. 28 Ref.
CODEN: DAZEA2 ISSN: 0011-9857
AVAIL. OF DOC.: Gedser Ring 14, 17493 Greifswald, Germany. (E-mail: ruth.menzel@greifswald.netsurf.de).
LANGUAGE: German
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB New drugs available for the treatment of diabetes mellitus are reviewed with reference to oral antidiabetics, drugs designed for weight regulation, and new insulin preparations. The possible development of new approaches to the treatment of patients with type II diabetes is discussed in relation to the heterogeneous nature of this disease.

L149 ANSWER 20 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-22273 DRUGU T E
TITLE: Insulin resistance syndrome: options for treatment.
AUTHOR: Granberry M C; Fonseca V A
CORPORATE SOURCE: Univ.Arkansas
LOCATION: Little Rock, Ark., USA
SOURCE: South.Med.J. (92, No. 1, 2-14, 1999) 1 Fig. 3 Tab. 123 Ref.
CODEN: SMJOAV ISSN: 0038-4348
AVAIL. OF DOC.: VA Medical Center (111J), 4300 W 7th St, Little Rock, AR 72205, U.S.A. (V.A.F.).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The mechanism and treatment of insulin (INS) resistance syndrome (IRS) is

reviewed. Polycystic ovary syndrome (PCOS) and the complications associated with IRS are also covered, discussing cardiovascular disease, hypertension and dyslipdemia. Treatment discussed includes weight reduction by dieting and exercise, metformin (MTF), **troglitazone** (TGZ), acarbose (ACB), etomoxir (ETM), and glimepiride (GMP), alone or **combined** with sulfonylureas (SNs). Treatment of IRS-associated disorders with drugs such as bile acid resins and naicin is also considered. In the event of lifestyle changes being ineffective, drugs are now available to lower plasma glucose by reducing INS resistance. Therapy aimed at preventing the development of diabetes mellitus (DM) is currently being investigated.

L149 ANSWER 21 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-42435 DRUGU T
TITLE: Approaches to the management of postprandial hyperglycemia.
AUTHOR: Landgraf R
CORPORATE SOURCE: Univ.Munich
LOCATION: Munich, Ger.
SOURCE: Exp.Clin.Endocrinol.Diabetes (107, Suppl. 4, S128-S132, 1999) 1 Tab. 70 Ref.
CODEN: ECEDF ISSN: 0947-7349
AVAIL. OF DOC.: Medizinische Klinik, Klinikum Innenstadt der LMU, Ziemssenstr. 1, 80336 Munich, Germany.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Approaches to the management of postprandial hyperglycemia are reviewed. Prevention and treatment of postprandial hyperglycemia includes: alpha-glucosidase inhibitors (acarbose, miglitol), biguanides (metformin), sulfonylureas, repaglinide, insulin analogues, glucagon-like peptide, **troglitazone**, orlistat and sibutramine. Treatment of type diabetes will be improved through the use of **combinations** of drugs with different modes of action. (conference paper: Satellite Symposium on Repaglinide: A New Dimension in the Management of Type 2 Diabetes, Barcelona, Spain, 1998). (No EX).

L149 ANSWER 22 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-29667 DRUGU T E S
TITLE: Sibutramine enhances weight loss and improves glycemic control and plasma lipid profile in obese patients with type 2 diabetes mellitus.
AUTHOR: Heath M J; Chong E; Weinstein S P; Seaton T B
LOCATION: Nottingham, U.K.
SOURCE: Diabetes (48, Suppl. 1, A308, 1999) 1 Tab.
CODEN: DIAEAZ ISSN: 0012-1797
AVAIL. OF DOC.: No Reprint Address.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The effects of sibutramine (Sib) 15 mg/day for 12 mth on weight loss were studied in a multicenter, randomized, double-blind, placebo-controlled trial in 236 obese patients (97 males, mean 54 yr) with type 2 diabetes. Improvements in **HbA1c**, fasting plasma glucose, triglycerides and HDL cholesterol with Sib were correlated with weight loss; 65% and 27% Sib treated patients lost at least 5% and 10% body weight, respectively. The pulse rate increased in Sib patients compared with placebo. The results suggest that Sib enhances weight loss in obese diabetic patients, which improves glycemic control and lipid parameters. (conference abstract: 59th Annual Scientific Sessions of the American Diabetes Association, San Diego, California, USA, 1999). (No EX).

L149 ANSWER 23 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1997-11763 DRUGU T E
TITLE: A case of Prader-Willi syndrome with long-term **mazindol** treatment.
AUTHOR: Inui A; Uemoto M; Takamiya S; Shibuya Y; Baba S; Kasuga M
LOCATION: Kobe, Jap.
SOURCE: Arch.Intern.Med. (157, No. 4, 464, 1997) 4 Ref.
CODEN: AIMDAP ISSN: 0003-9926
AVAIL. OF DOC.: No Reprint Address.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB **Mazindol** 1 mg/day, administered before lunch, reduced body weight by 5%, lowered **HbA1c** levels and prevented hyperglycemic coma in a 23-yr-old male with Prader-Willi syndrome and a 10-yr history of diabetes. The patient had been receiving insulin (Monotard human, Yamanouchi) 44 U/day. **Mazindol** had no side-effects. Nutritional treatment had been only transiently effective. (No EX).

L149 ANSWER 24 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1997-21731 DRUGU T P E S
TITLE: Oral antihyperglycaemics. Considerations in older patients with non-insulin-dependent diabetes mellitus.
AUTHOR: Jennings P E
LOCATION: York, U.K.
SOURCE: Drugs Aging (10, No. 5, 323-31, 1997) 3 Tab. 27 Ref.
ISSN: 1170-229X
AVAIL. OF DOC.: Diabetes Centre, York District Hospital, Wigginton Road, York Y)3 7HE, England.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Use of p.o. antihyperglycemics in the treatment of older patients with NIDDM is reviewed with reference to sulphonylureas, biguanides, alpha-glucosidase inhibitors, **combination** treatment with insulin, other p.o. agents (guar gum, dexfenfluramine) and compounds currently under investigation (repaglinide, thiazolinediones such as **troglitazone**, beta-3-adrenoceptor agonists, vanadium salts, amylin antagonists and glycogen-like peptide-1). Mechanism of action, adverse effects and pharmacokinetics are discussed.

L149 ANSWER 25 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1996-30628 DRUGU P B
TITLE: Responders and non-responders: treatment with the thiazolidinedione **insulin sensitizer**, BRL 49653, improves diabetic dyslipidemia more than reducing hyperglycemia in ZDF rats.
AUTHOR: Oliver W Jr; Boncek V; Wiard R; Brown K
LOCATION: Research Triangle Park, N.C., USA
SOURCE: Diabetes (45, Suppl. 2, 316A, 1996) 1 Tab.
CODEN: DIAEAZ ISSN: 0012-1797
AVAIL. OF DOC.: No reprint address.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB P.o. BRL-49653 improved dyslipidemia in male Zucker Diabetic Fatty (ZDF/GmiTM fa/fa) rats. Increasing the dose of BRL-49653 in non-responders to 15 mg/kg b.i.d. for an additional 10 days, did not decrease post-prandial plasma glucose (G), but improved the dyslipidemia. Intrascapular brown adipose tissue (BAT) weight was larger in responders,

suggesting that BAT metabolism may be linked to PPARgamma activation and G lowering in these animals. These data suggest that the in-vivo effects of PPARgamma activation has a greater effect on lipid metabolism and storage than on glucose disposal in the ZDF fa/fa rat. (conference abstract).

L149 ANSWER 26 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1996-30510 DRUGU P E
TITLE: Antidiabetic effects of PPARgamma activators are not enhanced by addition of beta3 adrenergic stimulation in db/db mice.
AUTHOR: Harrington W; Brown K; Hashim M; Faison W; Harper R; Sun F; Collins S
LOCATION: Research Triangle Park, N.C., USA
SOURCE: Diabetes (45, Suppl. 2, 75A, 1996)
CODEN: DIAEAZ ISSN: 0012-1797
AVAIL. OF DOC.: No Reprint Address.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The antidiabetic effects of the Peroxisome Proliferator-Activated Receptor gamma (PPARg) activator BRL-49653 (BRL) were not enhanced by addition of the beta3 receptor agonist CL-316243 (CL) in db/db diabetic mice. The increase in body weight with BRL alone was attenuated. This may be due to increased thermogenic capacity in BAT. (conference abstract).

L149 ANSWER 27 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1995-50558 DRUGU T E S
TITLE: Insulin resistance in systemic hypertension: pharmacotherapeutic implications.
AUTHOR: Mediratta S; Fozailoff A; Frishman W H
CORPORATE SOURCE: Albert-Einstein-Coll.; Mount-Sinai-Med.Cent.
LOCATION: New York, N.Y., USA
SOURCE: J.Clin.Pharmacol. (35, No. 10, 943-56, 1995) 3 Fig. 2 Tab. 162 Ref.
CODEN: JCPCBR ISSN: 0091-2700
AVAIL. OF DOC.: 1825 Eastchester Road, Bronx, NY 10461, U.S.A. (W.H.F.).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The pharmacotherapeutic implications of insulin resistance in systemic hypertension are reviewed. Mechanisms of hypertension with hyperinsulinemia, and treatment modalities, including the use of hypoglycemic drugs, including **pioglitazone**, **troglitazone** and **CS-045**, weight reducing agents, including fenfluramine, antihypertensive agents including bendroflumethiazide, hydrochlorothiazide, enalapril, captopril ramipril, metoprolol and prazosin, **combined** therapy, and the in-vitro effects of verapamil, diltiazem and nifedipine are discussed.

L149 ANSWER 28 OF 45 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1994-24327 DRUGU P B T E S
TITLE: New pharmacological approaches to insulin and lipid metabolism.
AUTHOR: Petrie J R; Donnelly R
CORPORATE SOURCE: Univ.Glasgow; Univ.Stanford
LOCATION: Glasgow, United Kingdom; Stanford, California, United States
SOURCE: Drugs (47, No. 5, 701-10, 1994) 5 Fig. 2 Tab. 44 Ref.
CODEN: DRUGAY ISSN: 0012-6667
AVAIL. OF DOC.: Department of Medicine and Therapeutics, Gardiner Institute, Western Infirmary, Glasgow G11 6NT, Scotland.

LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The new pharmacological approaches for the treatment of non-insulin-dependent diabetes mellitus (NIDDM) and obesity based on the manipulation of insulin and lipid metabolism are reviewed. Drugs being evaluated include **insulin-sensitizing agents**, inhibitors of FFA oxidation, stimulants of energy expenditure (beta-3 agonists), inhibitors of lipolysis and inhibitors of gluconeogensis.

L149 ANSWER 29 OF 45 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2000:15006 CAPLUS
DOCUMENT NUMBER: 132:73650
TITLE: **Insulin sensitizer** in **combination** with an **anorectic** for the treatment of **diabetes**
INVENTOR(S): Odaka, Hiroyuki; Yamane, Masahiro
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000195	A1	20000106	WO 1999-JP3496	19990629
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2329004	AA	20000106	CA 1999-2329004	19990629
AU 9942914	A1	20000117	AU 1999-42914	19990629
JP 2000080047	A2	20000321	JP 1999-183299	19990629
BR 9911656	A	20010320	BR 1999-11656	19990629
EP 1093370	A1	20010425	EP 1999-957622	19990629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6329403	B1	20011211	US 1999-380059	19990825
NO 2000006630	A	20010226	NO 2000-6630	20001222
US 2002086885	A1	20020704	US 2001-36208	20011229

PRIORITY APPLN. INFO.: JP 1998-183700 A 19980630
WO 1999-JP3496 W 19990629
US 1999-380059 A3 19990825

OTHER SOURCE(S): MARPAT 132:73650
AB A pharmaceutical compn. which comprises an insulin sensitizer in combination with an **anorectic**, which is useful as an agent for preventing or treating diabetes. Administration of **pioglitazone** -HCl in combination with **mazindol** to noninsulin-dependent diabetic mellitus patients provided an excellent blood sugar lowering action and a tendency to decrease body wt. as compared with administration of **pioglitazone**-HCl or **mazindol** alone.
IT **22232-71-9, Mazindol 112529-15-4, Pioglitazone** hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**insulin sensitizer** in combination with an

anorectic for the treatment of diabetes)
IT **9004-10-8, Insulin,** biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**insulin sensitizer** in combination with an **anorectic** for the treatment of diabetes)
IT **97322-87-7, Troglitazone 122320-73-4, Rosiglitazone 155141-29-0, Rosiglitazone** maleate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**insulin sensitizer** in combination with an **anorectic** for the treatment of diabetes)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L149 ANSWER 30 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:392237 CAPLUS
DOCUMENT NUMBER: 136:401651
TITLE: Preparation of fused pyridine derivatives as HMG-CoA reductase inhibitors
INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-Chi; Sun, Chong-Qing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 875,218.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002061901	A1	20020523	US 2001-8154	20011204
US 2002028826	A1	20020307	US 2001-875218	20010606

PRIORITY APPLN. INFO.: US 2000-211594P P 20000615
US 2001-875218 A2 20010606
OTHER SOURCE(S): MARPAT 136:401651
AB The title compds. I and their pharmaceutically acceptable salts, esters, prodrug esters, and stereoisomers are claimed [wherein: Z = CH(OH)CH2CR7(OH)CH2CO2R3 or corresponding pyranone lactone derivs.; n = 0, 1; x = 0, 1, 2, 3, or 4; y = 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0; and optionally one or more carbons of (CH2)x and/or (CH2)y together with addnl. carbons form a 3 to 7 membered spirocyclic ring; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H or lower alkyl; R4 = H, halo, CF3, OH, alkyl, alkoxy, CO2H, (un)substituted NH2, cyano, (un)substituted CONH2, etc.; R7 = H, alkyl]. The compds. are HMG-CoA reductase inhibitors, and are active in inhibiting cholesterol biosynthesis and modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol (no data). I are thus useful in treating hyperlipidemia and dyslipidemia, in hormone replacement therapy, and in treating hypercholesterolemia, hypertriglyceridemia and atherosclerosis, as well as Alzheimer's disease and osteoporosis. Prepns. of several compds. are described. For instance, a multistep synthesis of fused pyridine deriv. II is reported. Compds. I may be used in a manner similar to atorvastatin, pravastatin, simvastatin, etc. Combinations of compds. I with various other drugs are claimed, the latter being specified as certain pharmacol. classes, as inhibitors of specific enzymes, as (ant)agonists of specific receptors, and as numerous named drugs.
IT **97322-87-7, Troglitazone 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic compns. also contg.; prepn. of fused pyridine derivs. as HMG-CoA reductase inhibitors)

L149 ANSWER 31 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:816444 CAPLUS
DOCUMENT NUMBER: 135:352829
TITLE: **Combination** therapeutic compositions containing benzene compounds
INVENTOR(S): Jaen, Juan C.; Chen, Jin-Long
PATENT ASSIGNEE(S): Tularik Inc., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001082916	A2	20011108	WO 2001-US14393	20010502
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002037928	A1	20020328	US 2001-847887	20010502

PRIORITY APPLN. INFO.: US 2000-201613P P 20000503
OTHER SOURCE(S): MARPAT 135:352829

AB The present invention provides pharmaceutical compns. and methods for the treatment of diabetes mellitus using combination therapy. The compns. relate to a benzene compd. and an antidiabetic agent such as sulfonylureas, biguanides, glitazones, .alpha.-glucosidase inhibitors, potassium channel antagonists, aldose reductase inhibitors, glucagon antagonists, activators of RXR, insulin therapy or other anti-obesity agent. The methods include the administration of the combination of benzene compd. with antidiabetic agent where the two components are delivered in a simultaneous manner, where the benzene compd. is administered first, followed by the antidiabetic agent, as well as wherein the antidiabetic agent is delivered first followed by the benzene compd. For example, the benzene compd. (I) was synthesized using a 5-amino-2-(3-chloro-5-pyridyloxy)benzonitrile (0.457 g) in methylene chloride to which was added 2,4-dichlorobenzenesulfonyl chloride (0.456 g), followed by pyridine (150 .mu.L). The reaction progress was monitored by TLC, and upon completion the solvent was removed under vacuum. The resulting residue was partitioned between methylene chloride and water. The org. layer was drawn off and concd. The residue was triturated with ether to provide 0.447 g of I as a white solid, m.p. 154-156.degree..

IT **97322-87-7, Troglitazone 106650-56-0,** Sibutramine **111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzene compds. in combination therapy for diabetes and diabetes-related disorders)

L149 ANSWER 32 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:713361 CAPLUS
DOCUMENT NUMBER: 135:257344
TITLE: Sulfur substituted naphthyldifluoromethylphosphonic acids as PTP-1B inhibitors

Searched by Barb O'Bryen, STIC 308-4291

INVENTOR(S): Bayly, Christopher; Ohkubo, Mitsuru
PATENT ASSIGNEE(S): Merck Frosst Canada + Co., Can.; Banyu Pharmaceutical Co., Ltd.
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070754	A1	20010927	WO 2001-CA374	20010321
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002002149	A1	20020103	US 2001-813499	20010321
US 2002091104	A1	20020711	US 2001-813489	20010321

PRIORITY APPLN. INFO.: US 2000-191369P P 20000322
OTHER SOURCE(S): MARPAT 135:257344

AB The invention encompasses the novel class of I, or a pharmaceutically acceptable salt or prodrug thereof, which are inhibitors of the protein tyrosine phosphatase-1B (PTP-1B) enzyme (no data). The invention also encompasses pharmaceutical compns. and methods of treating or preventing PTP-1B mediated diseases, including diabetes. In I, each X1 = H, OH, halogen, CN, CO2H, CO2C1-6alkyl, CO2C2-6alkenyl, OC1-6alkyl, OC2-6alkenyl, C(O)C1-6alkyl, C(O)C2-6alkenyl, OC(O)C1-6alkyl, OC(O)C2-6alkenyl, S(O)xC1-6alkyl, S(O)xC2-6alkenyl, C1-6 alkyl, C2-6alkenyl, S(O)2NR1R2, C(O)NR1R2, and NR1R2, wherein each alkyl group and each alkenyl group in each substituent is optionally substituted. X1, CF2P(O)(OR5)2 and Y1S(O)xR are substituted onto any position of either ring; each x = 0-2; R5 = H. R1 and R2 independently = H and C1-4alkyl, wherein said alkyl substituents are optionally substituted with 1-9 halogen atoms; Y1 = bond, C1-4 alkylene group, and C2-4 alkenylene group, wherein said alkylene group and said alkenylene group are optionally substituted. R = C1-10 alkyl, C2-10alkenyl, C2-10alkadienyl, C2-10alkynyl, Ar1, and Het1, wherein said alkyl, alkenyl, alkadienyl, and alkynyl are optionally substituted; Het1 = a 5-10 membered arom. ring system comprising 1 ring or 2 rings fused together and 1-4 heteroatoms selected from O, N, S(O)x, and combinations thereof, and 0-2 carbonyl groups, wherein one of said fused rings is optionally a benzene ring, and said Het1 is optionally substituted; Ar1 = Ph or naphthyl, optionally substituted. Although the methods of prepn. are not claimed, the 12-step prepn. of [7-[4-(difluorophosphonomethyl)benzylthiomethyl]naphthalen-2-yl]difluoromethylphosphonic acid is described.

IT **9004-10-8, Insulin**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and **sensitizers** and mimetics combined with sulfur-substituted naphthyldifluoromethylphosphonic acids for treating, controlling or preventing diabetes or obesity)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L149 ANSWER 33 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:713360 CAPLUS
DOCUMENT NUMBER: 135:273076
TITLE: Sulfur substituted phenyldifluoromethylphosphonic

acids as PTP-1B inhibitors
INVENTOR(S): Li, Chun Sing; Lau, Cheuk K.; Therien, Michel; Gauthier, Jacques Y.; Bayly, Christopher; Dufresne, Claude; Fortin, Rejean; Leblanc, Yves; Roy, Patrick; Wang, Zhaoyin
PATENT ASSIGNEE(S): Merck Frosst Canada + Co., Can.
SOURCE: PCT Int. Appl., 337 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070753	A1	20010927	WO 2001-CA373	20010321
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002002149	A1	20020103	US 2001-813499	20010321
US 2002091104	A1	20020711	US 2001-813489	20010321

PRIORITY APPLN. INFO.: US 2000-191369P P 20000322
OTHER SOURCE(S): MARPAT 135:273076

AB The invention encompasses the novel class of I (e.g. 4'-[4-(difluorophosphonomethyl)benzylthiomethyl]-4-(3-methylbutoxy)biphenyl-3-ylphosphonic acid), or a pharmaceutically acceptable salt or prodrug thereof, which are inhibitors of the protein tyrosine phosphatase-1B (PTP-1B) enzyme (no data). The invention also encompasses pharmaceutical compns. and methods of treating or preventing PTP-1B mediated diseases, including diabetes. In I, X1 and X2 = independently H, OH, halogen, CN, CO2H, CO2C1-6alkyl, CO2C2-6alkenyl, OC1-6alkyl, OC2-6alkenyl, C(O)C1-6alkyl, C(O)C2-6alkenyl, OC(O)C1-6alkyl, OC(O)C2-6alkenyl, S(O)xC1-6alkyl, S(O)xC2-6alkenyl, C1-6 alkyl, C2-6alkenyl, C2-6alkynyl, S(O)2NR1R2, C(O)NR1R2, and NR1R2, wherein each alkyl group and each alkenyl group in each substituent is optionally substituted. X = 0-2; R5 = H. R1 and R2 independently = H and C1-4alkyl, wherein said alkyl substituents are optionally substituted with 1-9 halogen atoms; Y1 = bond, C1-6 alkylene group, and C2-6 alkenylene group, wherein said alkylene group and said alkenylene group are optionally substituted. R = C1-10 alkyl, C2-10alkenyl, C2-10alkadienyl, C2-10alkynyl, Ar1, and Het1, wherein said alkyl, alkenyl, alkadienyl, and alkynyl are optionally substituted; Het1 = a 5-10 membered arom. ring system comprising 1 ring or 2 rings fused together and 1-4 heteroatoms selected from O, N, S(O)x, and combinations thereof, and 0-2 carbonyl groups, wherein one of said fused rings is optionally a benzene ring, and said Het1 is optionally substituted; Ar1 = Ph or naphthyl, optionally substituted. Although the methods of prepn. are not claimed, 209 example prepns. are included.

IT **9004-10-8**, **Insulin**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and **sensitizers** and mimetics combined with sulfur-substituted phenyldifluoromethylphosphonic acids for treating, controlling or preventing diabetes or obesity)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L149 ANSWER 34 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:617987 CAPLUS

DOCUMENT NUMBER: 135:180757
TITLE: Preparation of 1,2-benzoxazolyloxyacetic acids and analogs as PPAR agonists for treatment of **diabetes** and lipid disorders
INVENTOR(S): Liu, Kun; Xu, Libo; Jones, A. Brian
PATENT ASSIGNEE(S): Merck + Co. Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060807	A1	20010823	WO 2001-US4636	20010214

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-183593P P 20000218
OTHER SOURCE(S): MARPAT 135:180757

AB The title compds. (I) [wherein R1 and R2 = independently H, F, (halo)alkyl, (halo)alkenyl, (halo)alkynyl; or R1 and R2 may form a cycloalkyl group; R3 and R4 = independently (fluoro)alkyl, (fluoro)alkenyl, (fluoro)alkynyl, or Cl; X = N or CR; Y = O, S, nor NR; Z = O or S; R = independently H or optionally fluoro- or alkoxy-substituted (cyclo)alkyl(oxy), alkenyl(oxy), or alkynyl(oxy); R5 = H or (un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heterocyclyl(oxy), etc.; and pharmaceutically acceptable salts and prodrugs thereof] were prepd. For example, 2,4-dihydroxy-3,5-dipropyl-1',1',1'-trifluoroacetophenone oxime was acetylated and then treated with pyridine and TEA to give 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. Etherification with Me .alpha.-bromoisobutyrate in the presence of Cs2CO3 in DMF, followed by sapon., afforded the 1,2-benzoxazolyloxyacetic acid (II). I are potent agonists of peroxisome proliferator activated receptor (PPAR) .alpha. and/or .gamma. and are useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR.alpha. and/or .gamma. mediated diseases, disorders, and conditions (no data).

IT **97322-87-7, Troglitazone 106650-56-0,** Sibutramine **111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration with; prepn. of benzisoxazolyloxyacetic acid PPAR agonists via cyclization of dihydroxyacetophenone oximes for treatment of diabetes and lipid disorders)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L149 ANSWER 35 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:472729 CAPLUS
DOCUMENT NUMBER: 135:56101
TITLE: Aromatic phosphonates as protein tyrosine phosphatase

1B (PTP-1B) inhibitors
INVENTOR(S): Leblanc, Yves; Dufresne, Claude; Gauthier, Jacques Yves; Young, Robert
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046204	A1	20010628	WO 2000-CA1548	20001221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002052347	A1	20020502	US 2000-745220	20001221

PRIORITY APPLN. INFO.: US 1999-171427P P 19991222
OTHER SOURCE(S): MARPAT 135:56101
AB The invention provides arom. phosphonates which are inhibitors of PTP-1B. The invention also encompasses pharmaceutical compns. and methods of treating or preventing PTP-1B-mediated diseases, including diabetes, obesity, and diabetes-related diseases. Prepn. of [2-bromo-4-(2-(3-bromo-4-(difluoro(phosphono)methyl)benzyl)-3-oxo-2,3-diphenylpropyl)phenyl](difluoro)methylphosphonic acid is described.
IT **97322-87-7, Troglitazone 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(arom. phosphonates as protein tyrosine phosphatase 1B inhibitors, therapeutic use prepn., pharmaceutical compns., and use with other agents)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L149 ANSWER 36 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:283949 CAPLUS
DOCUMENT NUMBER: 134:311218
TITLE: Synthesis and use of heterocyclic sodium/proton exchange inhibitors
INVENTOR(S): Ahmad, Saleem; Wu, Shung C.; O'Neil, Steven V.; Ngu, Khehyong; Atwal, Karnail S.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027107	A2	20010419	WO 2000-US27461	20001002
WO 2001027107	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-158755P P 19991012
OTHER SOURCE(S): MARPAT 134:311218

AB Compds. of formula I [wherein; n is 1-5; X is N or CR5, where R5 is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl; Z is a heteroaryl group; R1 is H, alk(en)(yn)yl, alk(enyl)(ynyl)oxy, (aryl or alkyl)3Si, cycloalk(en)yl, (aryl)amino, aryl(alkyl), cycloheteroaryl, etc.; R2, R3 and R4 are any of the groups set out for R1 and optionally substituted with 1 to 5 substituents which may be the same or different and when X is N, R1 is preferably aryl or heteroaryl] are claimed. Several hundred examples are disclosed. Synthesis of II proceeds via cyclopropanation of the cinnamate derived from the olefination between 3,5-dichlorobenzaldehyde and t-butyldiethylphosphonoacetate. The intermediate tert-Bu ester is converted to the corresponding .alpha.-chloroketone and reacted with acetyl guanidine to provide II in a total of 5 steps. Compds. I are said to be sodium/proton exchange inhibitors (NHE). Pharmaceutical combinations are claimed using I and certain antihypertensive agents, .beta.-adrenergic agonists, hypolipidemic agents, antidiabetic agents, antiobesity agents, etc. Compds. I are useful as antianginal and cardioprotective agents and provide a method for preventing or treating angina pectoris, cardiac dysfunction, myocardial necrosis, and arrhythmia.

IT **9004-10-8, Insulin**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(or **sensitizers**, pharmaceuticals also contg.; synthesis and use of heterocyclic sodium/proton exchange inhibitors)

IT **97322-87-7, Troglitazone 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals also contg.; synthesis and use of heterocyclic sodium/proton exchange inhibitors)

L149 ANSWER 37 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:709687 CAPLUS
DOCUMENT NUMBER: 135:272869
TITLE: Synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 **diabetes**
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319

PRIORITY APPLN. INFO.: US 2000-191381P P 20000322
OTHER SOURCE(S): MARPAT 135:272869
AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH2, CH-alkyl when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6- or 7-NO2, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R2 = H; R3 = H, alkyl; R4 = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R5 = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R7 = H, F, alkyl; or R5 and R7 can be taken together to be oxo; R6 = carboxy, alkoxycarbonyl, amido, acyl, alkyl, OH, alkoxy; R9 = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prepd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBt, EDC, room temp.) to give amide II. Compds. I are glycogen phosphorylase inhibitors used for treating type 2 diabetes mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-glycogen phosphorylase inhibiting anti-diabetic agents are also claimed.
IT **97322-87-7, Troglitazone 106650-56-0,** Sibutramine **111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical in combination with; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

L149 ANSWER 38 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:197392 CAPLUS
DOCUMENT NUMBER: 128:275081
TITLE: Use of sibutramine analogs to prevent the development of **diabetes**
INVENTOR(S): Bailey, Clifford James; Jones, Robert Brian; Jackson, Helen Christine
PATENT ASSIGNEE(S): Knoll Aktiengesellschaft, Germany; Bailey, Clifford James; Jones, Robert Brian; Jackson, Helen Christine
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811884	A1	19980326	WO 1997-EP5039	19970915
W: AL, AU, BG, BR, BY, CA, CN, CZ, GE, HU, IL, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9747740	A1	19980414	AU 1997-47740	19970915
AU 724488	B2	20000921		
EP 927028	A1	19990707	EP 1997-910288	19970915
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9711517	A	19990824	BR 1997-11517	19970915
CN 1237905	A	19991208	CN 1997-199787	19970915
JP 2001503737	T2	20010321	JP 1998-514271	19970915
ZA 9708450	A	19990319	ZA 1997-8450	19970919
US 6174925	B1	20010116	US 1999-254924	19990317
NO 9901358	A	19990319	NO 1999-1358	19990319

PRIORITY APPLN. INFO.: GB 1996-19757 A 19960921
WO 1997-EP5039 W 19970915
OTHER SOURCE(S): MARPAT 128:275081

AB A compd. of formula (I) or a pharmaceutically acceptable salt thereof in which R1 and R2 are independently H or Me (for example N,N-dimethyl-1-[1-(4-chlorophenyl)cyclobutyl]-3-methylbutylamine hydrochloride optionally in the form of its monohydrate) is used for reducing insulin resistance in humans in whom impaired glucose tolerance and non-insulin-dependent diabetes mellitus have not yet presented.

IT **84485-00-7 97322-87-7, Troglitazone 106650-56-0D**, Sibutramine, analogs **111025-46-8, Pioglitazone 125494-59-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(use of sibutramine analogs to prevent the development of diabetes)

L149 ANSWER 39 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:228137 CAPLUS
DOCUMENT NUMBER: 124:251099
TITLE: Chromium and other **insulin sensitizers** may enhance glucagon secretion: implications for hypoglycemia and weight control
AUTHOR(S): McCarty, M. F.
CORPORATE SOURCE: San Diego, CA, 92109, USA
SOURCE: Med. Hypotheses (1996), 46(2), 77-80
CODEN: MEHYDY; ISSN: 0306-9877
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 35 refs. Increased pancreatic beta-cell secretory activity usually is assocd. with decreased alpha-cell activity; stimulated beta-cells release gamma-aminobutyric acid, which hyperpolarizes alpha-cells, inhibiting glucagon release. Thus, insulin secretion and glucagon secretion are usually inversely coupled. This suggests that chromium and other insulin-sensitizing modalities, by down-regulating beta-cell activity, may increase glucagon secretion. Such an effect might play a role in the documented therapeutic activity of supplemental chromium and biguanides in reactive hypoglycemia, and might also be of benefit to dieters.

IT **9004-10-8, Insulin**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**sensitizers**; chromium and other **insulin sensitizers** enhancement of glucagon secretion in relation to hypoglycemia and wt. control)

L149 ANSWER 40 OF 45 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001403276 EMBASE
TITLE: Controlling postprandial hyperglycemia.
AUTHOR: Ratner R.E.
CORPORATE SOURCE: Dr. R.E. Ratner, Medstar Research Institute, 650 Pennsylvania Avenue SE, Washington, DC 20003-4393, United States
SOURCE: American Journal of Cardiology, (26 Jul 2001) 88/6 SUPPL. 1 (26H-31H).
Refs: 42
ISSN: 0002-9149 CODEN: AJCDAG
PUBLISHER IDENT.: S 0002-9149(01)01834-3
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A growing body of evidence indicates that measurements of postprandial glucose levels, in combination with glycosylated hemoglobin, are a more accurate predictor of metabolic abnormality than fasting or preprandial glucose levels for individuals with type 2 diabetes. Early identification of elevated postprandial blood glucose levels is an important step in predicting the onset of microvascular and macrovascular complications that can progress to full symptomatic diabetes. This article summarizes the research conducted to date on the diagnostic import of postprandial glucose and the parameters established for judging the need for treatment. When individuals cannot reach target glucose levels through diet and exercise, medical treatment is necessary. The article reviews a range of treatment options, including insulin secretagogues, **insulin sensitizers**, antiabsorptive agents, weight reduction agents, and insulin and combination medical therapy. .COPYRGT. 2001 by Excerpta Medica, Inc.

L149 ANSWER 41 OF 45 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95248469 EMBASE
DOCUMENT NUMBER: 1995248469
TITLE: American Diabetes Association Scientific Sessions, 1995: Non-insulin- dependent diabetes mellitus.
AUTHOR: Bloomgarden Z.T.
SOURCE: Diabetes Care, (1995) 18/8 (1215-1219).
ISSN: 0149-5992 CODEN: DICAD2
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L149 ANSWER 42 OF 45 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-291951 [33] WPIDS
DOC. NO. CPI: C2002-085735
TITLE: Use of a selective cGMP phosphodiesterase-5 inhibitor for treatment of insulin resistance syndrome including dyslipidemia, hypertension, type II diabetes mellitus, impaired glucose tolerance, atherosclerosis or truncal obesity.
DERWENT CLASS: B02
INVENTOR(S): FRYBURG, D A; GIBBS, E M; KOPPIKER, N P
PATENT ASSIGNEE(S): (FRYB-I) FRYBURG D A; (PFIZ) PFIZER INC; (PFIZ) PFIZER LTD
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002013798	A2	20020221	(200233)*	EN	60

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001076607 A 20020225 (200245)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002013798	A2	WO 2001-IB1428	20010806

AU 2001076607 A AU 2001-76607 20010806

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001076607 A	Based on	WO 200213798

PRIORITY APPLN. INFO: GB 2001-17134 20010713; US 2000-224928P 20000811; GB 2000-30649 20001215; US 2001-266083P 20010202; GB 2001-6465 20010315; GB 2001-6468 20010315

AB WO 200213798 A UPAB: 20020524

NOVELTY - Use of a selective cyclic guanosine monophosphate (cGMP) phosphodiesterase-5 (PDE-5) inhibitor (I) for curative, palliative or prophylactic treatment of insulin resistance syndrome (i.e. existence of 2 or more of dyslipidemia, hypertension, type II diabetes mellitus, impaired glucose tolerance (IGT), family history of diabetes, hyperuricemia and/or gout, a procoagulant state, atherosclerosis or truncal obesity, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) use of sildenafil for the preparation of a medicament for curative, palliative or prophylactic treatment of insulin resistance syndrome in a patient having dyslipidemia, hypertension, type II diabetes mellitus, impaired glucose tolerance (IGT) or family history of diabetes and truncal obesity;

(2) use of sildenafil in **combination** with other agents for the preparation of a medicament for curative, palliative or prophylactic treatment of insulin resistance syndrome in a patient having dyslipidemia, hypertension, type II diabetes mellitus, impaired glucose tolerance (IGT) or family history of diabetes and truncal obesity;

(3) a method of treating insulin resistance syndrome comprising administration of (I) or its salt, solvate or composition;

(4) a method of treating insulin resistance syndrome comprising administration of (I) in **combination** with 1 or more protein kinase inhibitors, activators or AMP-activated protein kinases, weight loss agents, insulin, peroxisome proliferator-activated receptor (PPAR)-alpha agonists, PPAR- alpha /PPAR- gamma agonists, sorbitol dehydrogenase inhibitors, aldose reductase inhibitors, **insulin sensitizing agents** and/or hypoglycemic agents;

(5) use of a selective pyrazolopyrimidinone cGMP PDE-5 inhibitor for the treatment of IGT; and

(6) a method of treating insulin resistance syndrome comprising administration of (I), preferably sildenafil, in **combination** with 1 or more weight loss agents, sulfonylureas, insulin, Rezulin, Avandia, Actos, Glipizide, Metformin, Acarbose, **rosiglitazone**, **pioglitazone**, farglitazar, LY333531, CS011, PPAR- alpha agonists and/or CP-470711.

ACTIVITY - Antidiabetic; Antilipemic; **Anorectic**; Antiarteriosclerotic; Uropathic; Hypotensive; Antigout; Vasotropic; Anticoagulant.

In a clinical trial in adults with diabetes mellitus, patients were treated chronically with Viagra (RTM; sildenafil citrate) in an out-patient multicenter study. Subjects were taking several different glucose lowering agents (including metformin, insulin or sulfonylureas) or were treated with diet alone. **Glycosylated hemoglobin (HbA1c)**, a recognized measure of chronic glucose control, was determined prior to the study. Significant improvements in glucose control was observed in patients treated with Viagra (RTM). Improvements were consistently observed across the subject group irrespective of their background therapy.

MECHANISM OF ACTION - cGMP PDE-5 Inhibitor.

(I) had an IC50 value of less than 100 nM against PDE-5 and a selectivity ratio of PDE-5 over PDE-3 of more than 100 (claimed).

USE - (I) Is useful for curative, palliative or prophylactic treatment of insulin resistance syndrome (i.e. existence of 2 or more of dyslipidemia, hypertension, type II diabetes mellitus (preferred), impaired glucose tolerance (IGT) (preferred), family history of diabetes, hyperuricemia and/or gout, a procoagulant state, atherosclerosis, or truncal obesity (claimed).
Dwg.0/0

L149 ANSWER 43 OF 45 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-371496 [40] WPIDS
DOC. NO. CPI: C2002-105072
TITLE: New somatostatin analog in optionally protected form useful in treatment of e.g. diabetes, tumors, chronic allograft rejection, angioplasty, inflammatory bowel disease, psoriasis.
DERWENT CLASS: B02
INVENTOR(S): ALBERT, R; BAUER, W; BODMER, D; BRUNS, C; FELNER, I; HELLSTERN, H; LEWIS, I; MEISENBACH, M; WECKBECKER, G; WIETFELD, B
PATENT ASSIGNEE(S): (NOVS) NOVARTIS AG; (NOVS) NOVARTIS-ERFINDUNGEN VERW GES MBH
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002010192	A2	20020207	(200240)*	EN	25
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001089778	A	20020213	(200240)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002010192	A2	WO 2001-EP8824	20010730
AU 2001089778	A	AU 2001-89778	20010730

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001089778	A	Based on	WO 200210192

PRIORITY APPLN. INFO: GB 2000-18891 20000801
AB WO 200210192 A UPAB: 20020626
NOVELTY - Somatostatin analog, cyclo((4-(NH2-C2H4-NH-CO-O)Pro)-Phg-DTrp-Lys-Tyr(4-Bzl)-Phe) (I) in optionally protected form is new.
DETAILED DESCRIPTION - Cyclo((4-(NH2-C2H4-NH-CO-O)Pro)-Phg-DTrp-Lys-Tyr(4-Bzl)-Phe) of formula (I) with one of the amino groups in optionally protected form and its salts and complexes are new.
Phg = -HN-CH(C6H5)-CO-; and
Bzl = benzyl.
INDEPENDENT CLAIMS are also included for the following:
(a) preparation of (I); and
(b) a pharmaceutical composition comprising (I) optionally in **combination** with an immunosuppressive agent, an anti-inflammatory agent, a GH secretogogue receptor modulating agent, a GH receptor antagonist, an insulin secretagogue (claimed), an insulin secretion

enhancer or an **insulin sensitizer** (disclosed).

ACTIVITY - Antiinflammatory; Cytostatic; Anti-HIV; Antidiabetic; Ophthalmological; Antithyroid; **Anorectic**; Antipsoriatic; Antirheumatic; Antiarthritic; Antidiarrheic; Vasotropic; Antiarteriosclerotic.

MECHANISM OF ACTION - Human somatostatin (hsst) receptor (preferably hsst1, hsst2, hsst3 or hsst5) binder; growth hormone (GH) secretagogue receptor binder; GH-release inhibitor; and IGF-1 plasma level inhibitor; angiogenesis inhibitor.

The IC50 (nMolar) of (I) towards binding assay of hsst1, hsst2, hsst3 and hsst5 was found to be 9.3 plus or minus 0.1, 1.0 plus or minus 0.1, 1.5 plus or minus 0.3 and 0.16 plus or minus 0.1 respectively.

USE - For the prevention or treatment of type I or II diabetes, acromegaly, angiopathy, diabetic proliferative retinopathy, diabetic macular edema, nephropathy, neuropathy and dawn phenomenon, insulin or glucagon release disorders, obesity (preferably morbid, hypothalamic or hyperinsulinemic), enterocutaneous and pancreaticocutaneous fistula, irritable bowel syndrome, Grave's disease, inflammatory bowel disease, psoriasis, rheumatoid arthritis, polycystic kidney disease, dumping syndrome, watery diarrhea syndrome, AIDS-related diarrhea, chemotherapy induced diarrhea, acute or chronic pancreatitis, gastrointestinal hormone secreting tumors (e.g. GEP tumors, vipomas, glucagonomas, insulinomas, carcinoids, etc), lymphocyte malignancies (e.g. lymphomas and leukemia), hepatocellular carcinoma, gastrointestinal bleeding (e.g. variceal oesophagial bleeding), malignant cell proliferative disease (e.g. cancer tumors), angiogenesis, inflammatory eye disease, cystoid macular edema, idiopathic cystoid macular edema, age-related macular degeneration, choroidal neovascularization related disorders and proliferative retinopathy.

(I) is also useful for preventing or combating graft vessel disease (e.g. allo- or xenotransplant vasculopathies, graft vessel atherosclerosis and transplant of heart, lung, liver and pancreas), preventing or treating vein graft stenosis, restenosis and/or vascular occlusion following vascular injury e.g. caused by catherization procedures or vascular scraping procedures (e.g. percutaneous transluminal angioplasty, laser treatment or other invasive procedures which disrupt the integrity of the vascular intima or endothelium), for in vivo detection of somatostatin receptor positive cells and tissues.

ADVANTAGE - (I) has an elimination half-life of 15-30 hours.

Dwg.0/0

L149 ANSWER 44 OF 45 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-354775 [37] WPIDS
DOC. NO. CPI: C2001-109826
TITLE: New aromatic compounds are melanin concentrating hormone antagonists, useful as anorectic agents, for treating or preventing obesity, also memory or hormonal disorders or diabetes.
DERWENT CLASS: B05
INVENTOR(S): ISHIHARA, Y; KATO, K; MORI, M; SHIMOMURA, Y; SUZUKI, N; TAKEKAWA, S; TERAUCHI, J
PATENT ASSIGNEE(S): (TAKE) TAKEDA CHEM IND LTD
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001021577	A2	20010329	(200137)*	EN	363

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AU AZ BA BB BG BR BY BZ CA CN CR CU CZ DM DZ EE GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LV MA MD MG MK MN MX MZ NO NZ PL RO RU SG SI SK TJ TM TR TT UA US UZ VN YU ZA

AU 2000073157 A 20010424 (200141)
JP 2002003370 A 20020109 (200208) 137

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001021577 A2		WO 2000-JP6375	20000919
AU 2000073157 A		AU 2000-73157	20000919
JP 2002003370 A		JP 2000-290357	20000920

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000073157 A	Based on	WO 200121577

PRIORITY APPLN. INFO: JP 2000-126272 20000420; JP 1999-266298 19990920; JP 1999-357889 19991216

AB WO 200121577 A UPAB: 20010704
NOVELTY - Novel aromatic compounds (I), which are melanin concentration hormone (MCH) antagonists.

DETAILED DESCRIPTION - Aromatic compounds of formula (I) and their salts are new:

Ar1 = an optionally substituted cyclic group;
X = a spacer having a main chain of 1-6 atoms;
Y' = a bond or a spacer having a main chain of 1-6 atoms;
Ar = a monocyclic aromatic ring which may be condensed with a 4-8 membered non-aromatic ring, and may be substituted;
R1, R2 = H or optionally substituted hydrocarbon; or
R1 and R2 together with the adjacent N may form = optionally substituted N-containing heterocyclic ring; or
R2 with Ar may form = a spiro ring ; or
R2 together with the adjacent N and Y' may form = an optionally substituted N-containing hetero ring.

INDEPENDENT CLAIMS are included for the following:

(a) new compounds (I'), i.e. (I) where Ar = a group of formula (i)-(v) each optionally substituted; n = 1-4; X = -CONR8c-, NR8cCO-, -CH=CH-CONR8c- or -SO2NR8c-; provided that: (a) Ar is (iii), (iv) or (v) when X is -SO2NH-, (b) Ar1 is not optionally substituted biphenylyl when X is -CONH- and Ar is benzopyran, dihydrobenzopyran, dihydrobenzoxazine, dihydrobenzoxazole or tetrahydrobenzoxazepine (excluding N-(2-(N,N-dimethylamino)methyl-6-tetralinyl)-4 biphenylylcarboxamide); and

(b) a composition comprising an MCH antagonist in **combination** with an agent for treating diabetes, hypertension, and/or arteriosclerosis.

R8C = H or 1-6C alkyl.

ACTIVITY - **Anorectic**; antidiabetic; nootropic; antiarteriosclerotic; hypotensive; .

MECHANISM OF ACTION - MCH antagonist; HMG-CoA reductase inhibitor; **insulin sensitizer**, insulin secretion enhancer; biguanide inhibitor; alpha -glucosidase inhibitor.

A test was carried out to determine antagonist activity of test compounds using membrane fractions from human and rat SLC-1 expressing CHO cells and (35S)-guanosine 5'-(gamma thio)triphosphate. N-(2-(N,N-dimethylamino)methyl-6-tetralinyl) (4'-methoxybiphenyl-4-yl)carboxamide had IC50 value 40 nM.

USE - (I) are useful as **anorectic** agents, for treating or preventing diseases caused by MCH, particularly obesity (claimed), also hyperphagia, emotional disorders, reproductive function disorders, memory disorders, dementia and hormonal disorders; or for treating or preventing diabetes, diabetic complications, arteriosclerosis or gonitis.

Dwg.0/0

L149 ANSWER 45 OF 45 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-548636 [50] WPIDS
DOC. NO. CPI: C2000-163694
TITLE: Composition comprising insulin sensitizer and fructose-1,6-bisphosphatase inhibitor, useful for the treatment of diabetes and diseases characterized by insulin resistance and/ or hyperglycemia, has synergistic effect.
DERWENT CLASS: B05
INVENTOR(S): ERION, M D; VAN POELJE, P; VANPOELJE, P
PATENT ASSIGNEE(S): (META-N) METABASIS THERAPEUTICS INC
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000038666	A2	20000706	(200050)*	EN	306
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW					
AU 2000020583	A	20000731	(200050)		
NO 2001003115	A	20010824	(200158)		
EP 1143955	A2	20011017	(200169)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
CZ 2001002353	A3	20011212	(200206)		
KR 2001099942	A	20011109	(200229)		
BR 9917005	A	20020402	(200231)		
SK 2001000917	A3	20020404	(200232)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000038666	A2	WO 1999-US30713	19991222
AU 2000020583	A	AU 2000-20583	19991222
NO 2001003115	A	WO 1999-US30713	19991222
		NO 2001-3115	20010621
EP 1143955	A2	EP 1999-964313	19991222
		WO 1999-US30713	19991222
CZ 2001002353	A3	WO 1999-US30713	19991222
		CZ 2001-2353	19991222
KR 2001099942	A	KR 2001-708102	20010623
BR 9917005	A	BR 1999-17005	19991222
		WO 1999-US30713	19991222
SK 2001000917	A3	WO 1999-US30713	19991222
		SK 2001-917	19991222

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000020583	A	Based on	WO 200038666
EP 1143955	A2	Based on	WO 200038666
CZ 2001002353	A3	Based on	WO 200038666
BR 9917005	A	Based on	WO 200038666
SK 2001000917	A3	Based on	WO 200038666

PRIORITY APPLN. INFO: US 1998-114718P 19981224
AB WO 200038666 A UPAB: 20001010

NOVELTY - A composition comprising an **insulin sensitizer** agent and an FBPase (fructose-1,6-bisphosphatase) inhibitor, or prodrugs or salts, is new.

ACTIVITY - Antidiabetic; hypoglycemic; **anorectic**; hypotensive; **synergist**.

Male Zucker Diabetic Fatty (ZDF) rats were purchased at 8 weeks of age and maintained under standard vivarium conditions (25 deg. C, 12-hour light, 12-hour dark cycle) and received powdered Purina 5008 chow and water ad libitum. At 11 weeks of age, animals with blood glucose greater than 500 mg/dl were selected and divided into 4 treatment groups (n = 5/group). The treatments were control, Troglitazone, (5-(2-amino-5-methylsulfanyl-thiazol-4-yl)-furan-2-yl)-phosphonic acid (G), and the **combination** of Troglitazone and (G). Drugs were administered as 0.2 % food admixtures for 15 days. The dose of Troglitazone selected (0.2 %) is a maximal dose, which in pilot studies was found to normalize blood glucose levels in 10-week old ZDF rats. It is higher than the dose reported to prevent the onset of hyperglycemia in prediabetic ZDF rats (Sreenan, et al. 1996). In animals with established diabetes such as those selected for this study, the effects of Troglitazone better approximate those in man, where modest glucose lowering effects are generally observed (Inzueehi et al. 1998). The dose of (G) selected (0.2 %) is also a maximal dose, a pilot study in the ZDF rat revealed that higher doses were of no additional benefit (blood glucose lowering at 0.5 % was equivalent to that at 0.2 %). Blood glucose levels were measured in tail vein samples by means of a HemoCue glucose analyzer. Values are expressed as the mean plus or minus the standard error of the mean. **Combination** treatment with troglitazone and (G) resulted in significantly greater reductions in blood glucose levels than treatment with either agent. In the control sample blood glucose was 762 plus or minus 31 mg/dl, for (G) 530 plus or minus 48, for troglitazone 431 plus or minus 73 and for the **combination** 222 plus or minus 39.

MECHANISM OF ACTION - PPAR (peroxisome proliferator-activated receptor)- gamma agonist; angiotensin converting enzyme inhibitor; renin inhibitor; angiotensin antagonist

USE - Used in the treatment of diabetes and diseases characterized by insulin resistance and/ or hyperglycemia, preferably obesity, hypertension or polycystic ovarian syndrome (claimed).

ADVANTAGE - The **combination** therapy results in decreases in hepatic glucose output beyond that observed for glucose lowering doses of the **insulin sensitizer** agent. The **combination** results in improvements in insulin resistance and/or insulin secretion beyond that observed for either agent alone.

Dwg.0/0

National Library of Medicine - Medical Subject Headings

2002 MeSH

MeSH Descriptor Data

Return to Entry Page

MeSH Heading	Hemoglobin A, Glycosylated
Tree Number	D09.203.408.375
Tree Number	D12.776.124.400.405.440
Tree Number	D12.776.422.512.380.440
Annotation	urine: coord IM with HEMOGLOBINURIA (IM); DF: note short X refs
Scope Note	Minor hemoglobin components of human erythrocytes designated A1a, A1b, and A1c. Hemoglobin A1c is most important since its sugar moiety is glucose covalently bound to the terminal amino acid of the beta chain. Since normal glycohemoglobin concentrations exclude marked blood glucose fluctuations over the preceding three to four weeks, the concentration of glycosylated hemoglobin A is a more reliable index of the blood sugar average over a long period of time.
Entry Term	Glycohemoglobin A
Entry Term	Glycosylated Hemoglobin A
Entry Term	Hb A1c
Entry Term	HbA1
Entry Term	Hemoglobin A(1)
Entry Term	Glycated Hemoglobins
Entry Term	Hb A1
Entry Term	Hb A1a+b
Entry Term	Hb A1a-1
Entry Term	Hb A1a-2
Entry Term	Hb A1b
Entry Term	Hemoglobin, Glycosylated
Entry Term	Hemoglobin, Glycosylated A1a-1
Entry Term	Hemoglobin, Glycosylated A1b
Allowable Qualifiers	AA AD AE AG AI AN BI CF CH CL CS CT DE DF DU EC GE HI IM IP ME PD PH PK PO RE SD SE ST TO TU UL UR
Entry Version	HBA GLYCOSYLATED
Registry Number	0
Previous Indexing	Hemoglobin A (1977-1981)
Previous Indexing	Hemoglobins (1966-1976)
History Note	82
Unique ID	D006442

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FILE 'CAPLUS' ENTERED AT 17:16:58 ON 22 JUL 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 22 Jul 2002  VOL 137 ISS 4
FILE LAST UPDATED: 21 Jul 2002  (20020721/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

L77 (      1245)SEA FILE=CAPLUS ABB=ON  GLYCOSYLAT?(3A)(HEMOGLOBIN#)
L78 (        76)SEA FILE=CAPLUS ABB=ON  L77(L)ANST/RL
L79 (      3134)SEA FILE=CAPLUS ABB=ON  HEMOGLOBINS/CT(L)ANT/RL
L80 (      5893)SEA FILE=CAPLUS ABB=ON  BLOOD GLUCOSE/OBI
L81           4 SEA FILE=CAPLUS ABB=ON  L78 AND L79 AND L80
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Roles
ANST = analytical study
ANT = analyte

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L83 (        76)SEA FILE=CAPLUS ABB=ON  L82(L)ANST/RL
L84 (      3134)SEA FILE=CAPLUS ABB=ON  HEMOGLOBINS/CT(L)ANT/RL
L85 (     43371)SEA FILE=CAPLUS ABB=ON  DIABETES MELLITUS/CT
L86 (       811)SEA FILE=CAPLUS ABB=ON  CONTROL?(L)L85
L87           1 SEA FILE=CAPLUS ABB=ON  L86 AND L83 AND L84

=> s (l81 or l87) not l145

L150          5 (L81 OR L87) NOT L145
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previously printed

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=> fil wpids

FILE 'WPIDS' ENTERED AT 17:16:59 ON 22 JUL 2002
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FILE LAST UPDATED: 17 JUL 2002              <20020717/UP>
MOST RECENT DERWENT UPDATE          200245   <200245/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been
    enabled in WPINDEX/WPIDS and WPIX  >>>

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>
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    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d que l107; s l107 not l146

L103(       116)SEA FILE=WPIDS ABB=ON  GLYCOS?(3A)(HAEMOGLOBIN# OR HEMOGLOBIN#)

L104(        68)SEA FILE=WPIDS ABB=ON  HBA1C
L105(       411)SEA FILE=WPIDS ABB=ON  (DIABETES OR GLUCOSE)(2A)CONTROL?
L106(   1073890)SEA FILE=WPIDS ABB=ON  S/DC - Derwent code - Instrumentation, Measuring, & Testing
L107           9 SEA FILE=WPIDS ABB=ON  (L103 OR L104) AND L105 AND L106


L151           9 L107 NOT (L146) previously printed

=> fil drugu; d que l144; s l144 not l147

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FILE LAST UPDATED: 17 JUL 2002      <20020717/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001.  <<<
>>>  (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION     <<<
>>>  SEE HELP COST                                        <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<


L143(      1302)SEA FILE=DRUGU ABB=ON  GLYCOSYLATED/CT AND HEMOGLOBIN/CT
L144          2 SEA FILE=DRUGU ABB=ON  L143 AND (QUANT. OR DET. OR ANALYSIS)/CT


L152           2 L144 NOT (L147) previously printed

=> fil medl; d que l28; s l28 not l148

FILE 'MEDLINE' ENTERED AT 17:17:03 ON 22 JUL 2002

 FILE LAST UPDATED: 20 JUL 2002 (20020720/UP).  FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2002 vocabulary.  Enter HELP THESAURUS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.
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L3          8046 SEA FILE=MEDLINE ABB=ON  HEMOGLOBIN A, GLYCOSYLATED/CT
L5        150205 SEA FILE=MEDLINE ABB=ON  DIABETES MELLITUS+NT/CT
L18         5920 SEA FILE=MEDLINE ABB=ON  L3(L)(AN OR CH)/CT
L20        11576 SEA FILE=MEDLINE ABB=ON  (GLUCOSE OR DIABETES)(3A)CONTROL?
L22         1648 SEA FILE=MEDLINE ABB=ON  L18/MAJ
L24        49564 SEA FILE=MEDLINE ABB=ON  L5(L)TH./CT
L25        29819 SEA FILE=MEDLINE ABB=ON  L24/MAJ
L26          122 SEA FILE=MEDLINE ABB=ON  L22 AND L25
L27           33 SEA FILE=MEDLINE ABB=ON  L20 AND L26
L28           11 SEA FILE=MEDLINE ABB=ON  L27 AND (HEMOGLOBIN OR HAEMOGLOBIN OR
                  HBA##)/TI
```

Subheading
AN - analysis
CH - chemistry
TH - therapy

```
L153          11 L28 NOT L148

=> fil embase; d que l46; d que l48; d que l50

FILE 'EMBASE' ENTERED AT 17:17:05 ON 22 JUL 2002
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 FILE COVERS 1974 TO 18 Jul 2002 (20020718/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L36         4020 SEA FILE=EMBASE ABB=ON  GLYCOSYLATED HEMOGLOBIN/CT OR GLYCOSYLA
                 TED HEMOGLOBIN A 1/CT OR GLYCOSYLATED HEMOGLOBIN A1C/CT
L42         2901 SEA FILE=EMBASE ABB=ON  DIABETES CONTROL/CT
L44           84 SEA FILE=EMBASE ABB=ON  L36/MAJ AND L42/MAJ
L45         5312 SEA FILE=EMBASE ABB=ON  HEMOGLOBIN DETERMINATION/CT
L46            4 SEA FILE=EMBASE ABB=ON  L44 AND L45


L36         4020 SEA FILE=EMBASE ABB=ON  GLYCOSYLATED HEMOGLOBIN/CT OR GLYCOSYLA
                 TED HEMOGLOBIN A 1/CT OR GLYCOSYLATED HEMOGLOBIN A1C/CT
L42         2901 SEA FILE=EMBASE ABB=ON  DIABETES CONTROL/CT
L44           84 SEA FILE=EMBASE ABB=ON  L36/MAJ AND L42/MAJ
L47        59161 SEA FILE=EMBASE ABB=ON  DIAGNOSTIC ACCURACY/CT
L48            5 SEA FILE=EMBASE ABB=ON  L44 AND L47


L36         4020 SEA FILE=EMBASE ABB=ON  GLYCOSYLATED HEMOGLOBIN/CT OR GLYCOSYLA
                 TED HEMOGLOBIN A 1/CT OR GLYCOSYLATED HEMOGLOBIN A1C/CT
L42         2901 SEA FILE=EMBASE ABB=ON  DIABETES CONTROL/CT
L44           84 SEA FILE=EMBASE ABB=ON  L36/MAJ AND L42/MAJ
L49        13995 SEA FILE=EMBASE ABB=ON  LABORATORY TEST/CT
L50            3 SEA FILE=EMBASE ABB=ON  L44 AND L49


=> s (l46 or l48 or l50) not l39

L154          10 (L46 OR L48 OR L50) NOT L39
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previously printed

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=> dup rem l153,l152,l150,l154,l151
FILE 'MEDLINE' ENTERED AT 17:17:36 ON 22 JUL 2002
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FILE 'DRUGU' ENTERED AT 17:17:36 ON 22 JUL 2002
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FILE 'CAPLUS' ENTERED AT 17:17:36 ON 22 JUL 2002
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FILE 'WPIDS' ENTERED AT 17:17:36 ON 22 JUL 2002
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PROCESSING COMPLETED FOR L153
PROCESSING COMPLETED FOR L152
PROCESSING COMPLETED FOR L150
PROCESSING COMPLETED FOR L154
PROCESSING COMPLETED FOR L151
L155 37 DUP REM L153 L152 L150 L154 L151 (0 DUPLICATES REMOVED)
ANSWERS '1-11' FROM FILE MEDLINE
ANSWERS '12-13' FROM FILE DRUGU
ANSWERS '14-18' FROM FILE CAPLUS
ANSWERS '19-28' FROM FILE EMBASE
ANSWERS '29-37' FROM FILE WPIDS

=> d ibib ab 1-37; fil hom

L155 ANSWER 1 OF 37 MEDLINE
ACCESSION NUMBER: 2001524207 MEDLINE
DOCUMENT NUMBER: 21455389 PubMed ID: 11571670
TITLE: Undiagnosed **diabetes** mellitus and metabolic **control** assessed by **HbA**(1c) among residents of nursing homes.
AUTHOR: Hauner H; Kurnaz A A; Haastert B; Groschopp C; Feldhoff K H
CORPORATE SOURCE: German Diabetes Research Institute at the Heinrich-Heine-University Dusseldorf, Germany.
SOURCE: EXPERIMENTAL AND CLINICAL ENDOCRINOLOGY AND DIABETES, (2001) 109 (6) 326-9.
Journal code: 9505926. ISSN: 0947-7349.
PUB. COUNTRY: Germany: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010926
Last Updated on STN: 20020122
Entered Medline: 20011205

AB AIMS/HYPOTHESIS: Diabetes prevalence and diabetes care in residents of nursing homes is a neglected area of research although the growing number of elderly people with diabetes represents a growing challenge for health care in most countries. In this study, we used HbA(1c) measurement to estimate the percentage of residents with undiagnosed diabetes and the quality of metabolic control of subjects with known diabetes in nursing homes. METHODS: All 41 nursing homes in the county of Heinsberg in Northrhine-Westfalia were asked to complete a structured questionnaire on the prevalence of known diabetes among all residents. In addition, all residents were offered measurement of glycated haemoglobin A1c (HbA(1c)) from a capillary blood sample. Undiagnosed diabetes was defined by a HbA(1c) level greater than 6.0%. RESULTS: 39 nursing homes participated in the study comprising 99.6% of all residents. Among the 1936 residents 507 (26.2%) were known to suffer from diabetes. Among the latter 37.0% were under insulin treatment. Blood samples for the determination of HbA(1c)

were obtained from 979 subjects from 20 nursing homes. Among those 60 years old or above (n = 843) the mean level of HbA(1c) in those with known diabetes was 7.3 +/- 1.5% and in those without 6.1 +/- 0.9%. Only 16.7% of the subjects with known diabetes had a HbA(1c) greater than 8.5% indicating poor metabolic control. Among the residents previously not known to have diabetes 47.2% had a HbA(1c) equal to or greater than 6.1%, but among those only 8.5% had a HbA(1c) greater than 7.0%. CONCLUSIONS/INTERPRETATION: Although the prevalence of undiagnosed diabetes mellitus defined by HbA(1c) above the normal range in elderly nursing home residents is high, only few may require treatment. The quality of metabolic control among those with known diabetes mellitus is better than expected.

L155 ANSWER 2 OF 37 MEDLINE
ACCESSION NUMBER: 2001056026 MEDLINE
DOCUMENT NUMBER: 20431524 PubMed ID: 10977012
TITLE: Therapy focused on lowering postprandial glucose, not fasting glucose, may be superior for lowering **HbA1c** . IOEZ Study Group.
COMMENT: Comment in: ACP Journal Club 2001 May-Jun;134(3):88
AUTHOR: Bastyr E J 3rd; Stuart C A; Brodows R G; Schwartz S; Graf C J; Zagar A; Robertson K E
CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana 46285, USA.. ejbIII@lilly.com
SOURCE: DIABETES CARE, (2000 Sep) 23 (9) 1236-41. Journal code: 7805975. ISSN: 0149-5992.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010813
Entered Medline: 20001221

AB OBJECTIVE: To compare the overall efficacy of combination therapies focused on fasting or postprandial blood glucose in patients with type 2 **diabetes** not adequately **controlled** with oral sulfonylurea agents alone. RESEARCH DESIGN AND METHODS: A total of 135 patients were randomly assigned for 3 months to 1 of 3 combination regimens with glyburide (G) that addressed postprandial blood glucose with insulin lispro (L+G), premeal blood glucose with metformin (M+G), or fasting blood glucose (FBG) with bedtime NPH insulin (NPH+G). RESULTS: At end point, HbAlc was significantly lower with all therapies (P = 0.001) and was significantly lower for L+G (7.68+/-0.88%) compared with either NPH+G (8.51+/-1.38%, P = 0.003) or M+G (8.31+/-1.31%, P = 0.025). FBG at end point was significantly lower for NPH+G (8.49+/-2.36 mmol/l) compared with either L+G (10.57+/-1.97 mmol/l, P = 0.001) or M+G (9.69+/-2.89 mmol/l, P = 0.029). The mean 2-h postprandial glucose after a test meal was significantly lower for L+G (10.87+/-2.88 mmol/l) versus NPH+G (12.21+/-3.12 mmol/, P = 0.052) or versus M+G (12.72+/-3.26 mmol/l, P = 0.009). The overall rate of hypoglycemia (episodes per 30 days) was low and not statistically significant between groups (P = 0.156). CONCLUSIONS: Adding a second antihyperglycemic agent, regardless of its timing of action, lowers HbAlc and glucose values. However, when insulin lispro was used to focus on postprandial blood glucose, there was a greater impact on overall metabolic control. These data support the importance of lowering postprandial blood glucose to optimize overall glycemic control and thus improve long-term outcomes.

L155 ANSWER 3 OF 37 MEDLINE
ACCESSION NUMBER: 2000418561 MEDLINE
DOCUMENT NUMBER: 20341037 PubMed ID: 10880892
TITLE: Improved blood glucose variability, **HbA1c** insuman Infusat and less insulin requirement in IDDM patients using insulin lispro in CSII. The Swedish Multicenter Lispro Insulin Study.
AUTHOR: Johansson U B; Adamson U C; Lins P E; Wredling R A
CORPORATE SOURCE: Department of Nursing, Division of Nursing Research at Karolinska Hospital, Karolinska, Institut, Stockholm, Sweden.. unn-britt.johansson@medks.ki.se
SOURCE: DIABETES AND METABOLISM, (2000 May) 26 (3) 192-6.
Journal code: 9607599. ISSN: 1262-3636.
PUB. COUNTRY: France
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000905

AB The aim of the study was to compare lispro (LP) and Insuman(R) (I) insulin in continuous subcutaneous insulin infusion (CSII) therapy with respect to blood **glucose control** as expressed by the standard deviation of blood glucose (SD(BG)) and HbA(1c) and to monitor the well-being (WBQ) and treatment satisfaction (DTSQ) parameters during such treatment. Forty-one IDDM patients who had used CSII for at least 6 months participated in an open-label, randomized, cross-over, multicenter study for 4 months (2 months LP and 2 months I or vice versa). Boluses with LP were given 5 min before each meal and with I 30 min before each meal. During LP administration compared with I, the SD(BG) of all blood glucose values (3.6 mmol/l vs. 3.9 mmol/l, p=0.012), as well as the SD(BG) of the postprandial, blood glucose values (3.6 mmol/l vs. 4.0 mmol/l, p=0.006), were significantly reduced. The HbA(1c) was significantly lower during LP administration (7.4% vs. 7.6%, p=0.047). The incidence of hypoglycemic events per 30 days (capillary blood glucose<3.0 mmol/l and/or symptoms) did not significantly differ between LP and I (9.7 vs. 8.0 per month, p=0.23). The total amount of daily insulin was slightly but significantly lower with LP, compared to I (38.0 IU vs. 40.3 IU, p=0.004). There was no treatment effects of LP compared to I concerning WBQ and DTSQ. It is concluded that in CSII therapy LP is superior to I with respect to the stability of blood **glucose control**, a lower HbA(1c), a less insulin requirement without increasing the frequency of hypoglycemia.

L155 ANSWER 4 OF 37 MEDLINE
ACCESSION NUMBER: 2000088121 MEDLINE
DOCUMENT NUMBER: 20088121 PubMed ID: 10624783
TITLE: Continuous glucose monitoring used to adjust diabetes therapy improves glycosylated **hemoglobin**: a pilot study.
COMMENT: Erratum in: Diabetes Res Clin Pract 2000 Mar;47(3):225
AUTHOR: Bode B W; Gross T M; Thornton K R; Mastrototaro J J
CORPORATE SOURCE: Atlanta Diabetes Associates, GA 30309, USA.
SOURCE: DIABETES RESEARCH AND CLINICAL PRACTICE, (1999 Dec) 46 (3) 183-90.
Journal code: 8508335. ISSN: 0168-8227.
PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000606
Entered Medline: 20000204

AB A 5-week pilot study was conducted to determine if continuous glucose monitoring could be used to improve glycemic control. A total of nine subjects with type 1 diabetes and HbA1c values greater than 8.5% completed the study. Subjects wore a continuous glucose monitor for two 1-week periods during the study. After each sensor use, changes to diet, insulin dosage and self-monitored blood glucose (SMBG) schedule were made. HbA1c decreased from 9.9% (S.D. = 1.1%) at baseline to 8.8% (S.D. = 1.0%) 5 weeks after baseline (P = 0.0006), but daily insulin usage was unchanged over the same period of time (P = 0.428). The glucose sensors performed accurately, with a median correlation of 0.92 and a mean absolute difference of 19.1% (S.D. = 9.0%). The continuous glucose profiles allowed identification of glucose patterns and excursions that helped direct changes in therapy. These treatment changes would not have been made on the basis of meter data alone and were effective in improving **glucose control**. Additional studies are needed to validate these findings. This pilot study highlights the potential for continuous glucose monitoring to provide the valuable information necessary to make therapy adjustments that can dramatically improve patients' glycemic control and reduce the risk of long-term complications.

L155 ANSWER 5 OF 37 MEDLINE
ACCESSION NUMBER: 97179924 MEDLINE
DOCUMENT NUMBER: 97179924 PubMed ID: 9028151
TITLE: Vitamin E modifies neither fructosamine nor **HbA1c** levels in poorly **controlled diabetes**.
AUTHOR: Gomez-Perez F J; Valles-Sanchez V E; Lopez-Alvarenga J C; Choza-Romero R; Ibarra Pascuali J J; Gonzalez Orellana R; Perez Ortiz O B; Rodriguez Padilla E G; Aguilar Salinas C A; Rull J A
CORPORATE SOURCE: Department of Diabetes and Lipid Metabolism, Instituto Nacional de la Nutricion Salvador Zubiran, Mexico, D.F.
SOURCE: REVISTA DE INVESTIGACION CLINICA, (1996 Nov-Dec) 48 (6) 421-4.
Journal code: 9421552. ISSN: 0034-8376.
PUB. COUNTRY: Mexico
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 19970507
Entered Medline: 19970428

AB OBJECTIVE: To examine the effects of vitamin E on total serum protein glycation (fructosamine), hemoglobin glycation (HbA1c), and serum levels of glucose, total cholesterol, triglycerides, LDL-C, HDL-C, apolipoprotein A1 and apolipoprotein B. MATERIAL AND METHODS: Sixty poorly controlled diabetic patients were randomly assigned to receive either 1200 mg/day of vitamin E or identical placebo capsules during a two month period following a double blind cross-over design with a four week wash-out period between regimens. RESULTS: Seven patients were excluded from the study because of reasons not related to the medication. In the remaining 53 patients, the levels of serum glucose, fructosamine, HbA1c, total cholesterol, HDL-C, LDL-C, Apo A1 and Apo B did not vary significantly with vitamin E as compared with placebo. CONCLUSIONS: No significant effects of vitamin E on any of the parameters evaluated were observed in poorly controlled diabetic patients.

L155 ANSWER 6 OF 37 MEDLINE
ACCESSION NUMBER: 94051810 MEDLINE
DOCUMENT NUMBER: 94051810 PubMed ID: 8234003
TITLE: [Measurement of glycosylated **hemoglobin** as a useful method for **controlling** type II **diabetes** mellitus in patients suspected of incomplete compensation].
Oznaczanie hemoglobiny glikozylowanej przydatna metoda kontroli przebiegu cukrzycy typu II u chorych podejrzanych o niepelne wyrownanie.
AUTHOR: Wywial M; Silanczyk A; Wywial R; Jakubowska D; Zmudzinski W; Kokot S
CORPORATE SOURCE: III Katedra, Akademii Medycznej, Katowicach.
SOURCE: POLSKIE ARCHIWUM MEDYCYNY WEWNETRZNEJ, (1993 Jul) 90 (1) 35-41.
Journal code: 0401225. ISSN: 0032-3772.
PUB. COUNTRY: Poland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Polish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931216

AB The conduction of levels of glycosylated hemoglobin in patients with type II diabetes mellitus was studied A group of 111 ambulant patients was analyzed and special attention paid to those patients who were given the highest permissible oral dose. The dependence between the achieved glycosylation tests results and types of therapy, the clinical course of diabetes mellitus, as well as the conduction of results of standard compensation tests was analyzed. A lower correlation degree between the level of HbA1 and the results of standard compensation tests was indicated. At the same time a high correlation degree between HbA1 and clinically proven diabetes complication progress was observed. All achieved results suggest the usefulness of HbA1 determination in patients with type II diabetes mellitus suspected of incomplete compensation for instance treated highest permissible oral dose.

L155 ANSWER 7 OF 37 MEDLINE
ACCESSION NUMBER: 88296067 MEDLINE
DOCUMENT NUMBER: 88296067 PubMed ID: 3042315
TITLE: Impact of SMBG on **control** of **diabetes** as measured by **HbA1**. 3-yr survey of a juvenile IDDM clinic.
AUTHOR: Belmonte M M; Schiffrin A; Dufresne J; Suissa S; Goldman H; Polychronakos C
CORPORATE SOURCE: Division of Endocrinology and Metabolism, McGill University, Montreal, Quebec, Canada.
SOURCE: DIABETES CARE, (1988 Jun) 11 (6) 484-8.
Journal code: 7805975. ISSN: 0149-5992.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198809
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880912

AB Three hundred twelve diabetic children and adolescents were seen in our diabetic clinic and instructed to test their capillary blood glucose (CBG) twice daily and to use an algorithm to adjust their short-acting insulin. Of this group, 219 youngsters had a full 3-yr period of observation. At each clinic visit, blood was obtained for fasting blood glucose and HbA1

and, once a year, cholesterol and triglycerides were also measured. Patient and parent accuracy in measuring CBG was found to be adequate. The changes over time in HbA1 were nondifferential across age and sex, and there was no difference in the level of HbA1 between age and sex groups, the number of tests reported to have been done by the patients, the number of injections of insulin per day, or the serum cholesterol. There was a significant relationship between the HbA1 and the fasting blood glucose (P less than .001) measured by the laboratory as well as with the serum triglyceride (P less than .01). The failure to improve diabetic control, despite measures that would have been expected to do so, was believed to relate more to a lack of compliance than to a flaw in the therapeutic approach. It was interesting to note that the adolescent patients in the study were in no worse control than the younger children in the group. Although better technical skills are available today to manage diabetes, the psychosocial approach to patient motivation requires improvement.

L155 ANSWER 8 OF 37 MEDLINE
ACCESSION NUMBER: 88017907 MEDLINE
DOCUMENT NUMBER: 88017907 PubMed ID: 3659877
TITLE: [**Control** of **diabetes** management: daily profile of blood glucose? self-monitoring of blood glucose? **HbA1/HbA1c**?].
Kontrolle der Diabeteseinstellung: Blutzuckertagesprofil? Blutzuckerselbstkontrolle? **HbA1/HbA1c**?.
AUTHOR: Diem P
CORPORATE SOURCE: Medizinische Universitatsklinik, Inselspital, Bern.
SOURCE: SCHWEIZERISCHE MEDIZINISCHE WOCHENSCHRIFT. JOURNAL SUISSE DE MEDECINE, (1987 Aug 4) 117 (31-32) 1191-5.
Journal code: 0404401. ISSN: 0036-7672.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198711
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19871116

AB The introduction of glucose oxidase strips has given blood glucose measurements a new dimension. Together with assessment of time-averaged blood glucose concentration by measurements of glycosylated hemoglobin, self-monitoring of blood glucose has proven of value in the management of diabetes mellitus in cases with intensified insulin therapy, at the beginning of insulin therapy, with frequent hyperglycemia, and a number of other management problems. The principles and information which are important for the interpretation of the two parameters are summarized.

L155 ANSWER 9 OF 37 MEDLINE
ACCESSION NUMBER: 86125021 MEDLINE
DOCUMENT NUMBER: 86125021 PubMed ID: 4090457
TITLE: [Informative significance of **hemoglobin** A1 in the **control** of **diabetes**].
Informativna stoinost na khemoglobin A1 pri provezhdane na diabetniia kontrol.
AUTHOR: Petrunova N; KamenovV; Tsanev A; Dochev D
SOURCE: VUTRESHNI BOLESTI, (1985) 24 (5) 77-83.
Journal code: 0032666. ISSN: 0506-2772.
PUB. COUNTRY: Bulgaria
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Bulgarian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198603
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321

Entered Medline: 19860318

AB Sixty one patients were studied, 23 with diabetes, type I and 38 with type II. The level of glycosilized hemoglobin was determined in all, corresponding to the routine battery of symptoms and laboratory data, used in the practice in the evaluation of the state of the diabetic patients. A low correlation coefficient was established (type I r = 0,1 and type II r = 0,1) between the calculated glucose and mean blood sugar from blood sugar profiles. Glycohemoglobin level under and over 10% was established both in patients with increased and normal blood sugar. The use of the routine control methods gave no possibility of objective evaluation for the state of metabolic diabetic disorders in all patients. The determination of glycosilized hemoglobin presented a possibility of obtaining unique information on metabolic compensation of diabetes and the effectiveness of the treatment applied.

L155 ANSWER 10 OF 37 MEDLINE
ACCESSION NUMBER: 85014733 MEDLINE
DOCUMENT NUMBER: 85014733 PubMed ID: 6237340
TITLE: [1 or several injections of insulin? Influence on the **control** of **diabetes** evaluated by glycosylated **hemoglobin** A1C].
Une ou plusieurs injections d'insuline? Influence sur le controle du diabete apprecie par l'hemoglobine glycosylee A1C.
AUTHOR: Wahl S; Moinade S
SOURCE: PRESSE MEDICALE, (1984 Sep 15) 13 (31) 1904-5.
Journal code: 8302490. ISSN: 0755-4982.
PUB. COUNTRY: France
Letter
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198411
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19841101

L155 ANSWER 11 OF 37 MEDLINE
ACCESSION NUMBER: 83104686 MEDLINE
DOCUMENT NUMBER: 83104686 PubMed ID: 6759078
TITLE: Metabolic control in 131 juvenile-onset diabetic patients as measured by **HbA1c**: relation to age, duration, C-peptide, insulin dose, and one or two insulin injections.
AUTHOR: Dahlquist G; Blom L; Bolme P; Hagenfeldt L; Lindgren F; Persson B; Thalme B; Theorell M; Westin S
SOURCE: DIABETES CARE, (1982 Jul-Aug) 5 (4) 399-403.
Journal code: 7805975. ISSN: 0149-5992.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198303
ENTRY DATE: Entered STN: 19900318
Last Updated on STN: 19900318
Entered Medline: 19830311

AB Glycosylated hemoglobin A (HbA1c), considered to reflect long-term metabolic **control** of **diabetes**, was analyzed in 131 patients, aged 2 5/12-19 6/12 yr, with juvenile-onset diabetes. Using stepwise multiple regression HbA1c, fasting blood glucose and plasma 3-hydroxybutyrate were analyzed as dependent variables versus independent variables such as age of the patients, duration of the disease, level of plasma immunoreactive C-peptide (IRCP), insulin dose, and number of insulin injections (one or two) per day. HbA1c was inversely related only to IRCP concentration. A low but significant, positive correlation was

found between HbA1c and the duration of diabetes. Stepwise addition of the other independent variables did not further increase the fraction of explained variance. HbA1c was also correlated with a subjective rating score of the metabolic control performed by the treating physician. Fasting plasma glucose was significantly related to HbA1c but not to any of the independent variables. Fasting 3-hydroxybutyrate showed an inverse correlation to the age of the patient. The present study showed that in juvenile-onset diabetic patients, endogenous insulin secretion as reflected by IRCP was the factor best correlated with a low level of HbA1c. After the cessation of endogenous insulin secretion, there is a progressive deterioration of metabolic control and multiple injections of insulin rather than one or two per day may be needed to reach optimal control in the patients.

L155 ANSWER 12 OF 37 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1986-40490 DRUGU P A E
TITLE: Effect of Short-Term Aspirin Therapy on Glycosylated Hemoglobin Analysis.
AUTHOR: Williams D R; Barmann D
LOCATION: Atlanta, Georgia, United States
SOURCE: Clin.Pharm. (5, No. 6, 508-10, 1986) 1 Tab. 12 Ref.
CODEN: CPHADV ISSN: 0278-2677
AVAIL. OF DOC.: Southern School of Pharmacy, Mercer University, Atlanta, GA, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT; MPC
FILE SEGMENT: Literature
AB Aspirin (AS) p.o. did not interfere with common clinical methods of determining glycosylated Hb (GHb) via HbA1, HbA1a, HbA1b and HbA1c in 10 nondiabetic subjects. Levels of salicylates (S) in blood were determined. A similar study is needed in diabetic subjects.

L155 ANSWER 13 OF 37 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1983-44371 DRUGU A
TITLE: Effect of Aspirin on Determinations of Glycosylated Hemoglobin.
AUTHOR: Nathan D M; Francis T B; Palmer J L
LOCATION: Boston, Massachusetts, United States
SOURCE: Clin.Chem. (29, No. 3, 466-69, 1983) 4 Fig. 17 Ref.
CODEN: CLCHAU ISSN: 0009-9147
AVAIL. OF DOC.: Diabetes Unit, Massachusetts General Hospital, Boston, MA 02114, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Acetylation of hemoglobin (Hb) by aspirin (Sigma) in vitro produced a minor fraction indistingusihable from glycosylated Hb by HPLC andelectrophoretic assays. Glycosylated Hb values determined by HPLC were elevated for 23 rheumatoid arthritis patients receiving high doses of aspirin. Ingestion of aspirin by a healthy volunteer resulted in apparent increases in glycosylated Hb determined by HPLC. Isoelectric focusing and colorimetric assays distinguished clearly between acetylated and glycosylated fractions. Measurement of acetylated Hb might be more useful than plasma salicylate as an index of chronic aspirin ingestion.

L155 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:143281 CAPLUS
DOCUMENT NUMBER: 132:191383
TITLE: An apparatus for monitoring **blood glucose** by detecting human hemoglobin and human glycosylated hemoglobin

Searched by Barb O'Bryen, STIC 308-4291

INVENTOR(S): Sonezaki, Shuji; Ohkami, Yumi
PATENT ASSIGNEE(S): Toto Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000065839	A2	20000303	JP 1998-254562	19980825

AB An immunosensor app. is provided for conveniently monitoring blood glucose at home by detecting human Hb and human glycosylated Hb. The app. comprises a sensor part equipped with a function to detect human Hb and a function to detect human glycosylated Hb, and a supply path for supplying a sample liq. to the sensor part. Upon supplying the sample liq. (e.g., urine), the blood glucose is easily monitored by immunol. measuring human Hb and human glycosylated Hb, and calcg. their ratio. Crosslinked Hbs are used as stable std. substances. Detailed description of diagrams for the app. assembly and the operation flow is given.

L155 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:573185 CAPLUS
DOCUMENT NUMBER: 134:190287
TITLE: Association of self-monitoring **blood glucose** profiles with glycosylated hemoglobin in patients with insulin-dependent diabetes
AUTHOR(S): Kovatchev, Boris P.; Cox, Daniel J.; Straume, Martin; Farhy, Leon S.
CORPORATE SOURCE: Department of Physiology, Center for Biomedical Imaging Technology, University of Connecticut Health Center, Framingham, CT, 06030, USA
SOURCE: Methods in Enzymology (2000), 321, 410-417
CODEN: MENZAU; ISSN: 0076-6879
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glycosylated Hb (Hb) is a marker for the glycemic control of individuals with insulin-dependent diabetes mellitus (IDDM). Numerous studies have investigated this relationship and found that glycosylated Hb generally reflects the av. blood glucose (BG) levels of an IDDM patient over the previous two months. A study was conducted to assess the accuracy of self-monitoring BGestimates of av. BG on the basis of a large data set contg. more than 300,000 SMBG readings of 608 individuals with diabetes, accompanied by HbA1c data. It was concluded that SMBG data account for about 50% of the variance of HbA1c. SMBG does not provide a very accurate representation of HbA1c, and should be used cautiously if an accurate est. of HbA1c is needed. However, SMBG can be clin. useful for a general categorical evaluation of HbA1c through a classification table. (c) 2000 Academic Press.

L155 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:620531 CAPLUS
DOCUMENT NUMBER: 131:240081
TITLE: Preparation of improved human hemoglobin calibrator, and its application to a biosensor and a toilet device for detecting hemoglobin or glycosylated hemoglobin in feces or a body fluid
INVENTOR(S): Sonezaki, Shuji; Yagi, Shinichi; Ogawa, Emika
PATENT ASSIGNEE(S): Toto Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF

Searched by Barb O'Bryen, STIC 308-4291

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11264824	A2	19990928	JP 1998-254561	19980825

PRIORITY APPLN. INFO.: JP 1998-20439 19980116

AB A highly sensitive and accurate calibrator for detecting human Hb is prepd. by stabilizing human Hb and suppressing the drop in its antigenicity due to the denaturation in a soln. The calibrator is formed by crosslinking human Hb either between two .alpha.-chains or two .beta.-chains using a specific crosslinking reagent. The crosslinked Hb does not undergo the dissocn. of subunits in comparison with unmodified Hb. The oxidn. rate of heme in Hb decreases upon crosslinking, and therefore, the rate of Hb denaturation caused by heme oxidn. is lowered. As a result, a highly sensitive and accurate antigen-antibody reactivity is maintained with the new human Hb calibrator for a long period. An immunol. surface plasmon resonance biosensor is constructed using this calibrator and applied to detecting human Hb derived from blood in feces or a body fluid. A toilet device equipped with this biosensor and an urine storage is built for detecting human Hb in urine. This method and app. can be applied to detecting glycosylated human Hb for the diagnosis of diabetes.

L155 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:133018 CAPLUS
DOCUMENT NUMBER: 130:349334
TITLE: Diagnostic utility of glycosylated hemoglobin concentrations in the cat
AUTHOR(S): Hoenig, M.; Ferguson, D. C.
CORPORATE SOURCE: Department of Physiology and Pharmacology, College of Veterinary Medicine, The University of Georgia, Athens, GA, 30602-7389, USA
SOURCE: Domestic Animal Endocrinology (1999), 16(1), 11-17
CODEN: DANEEE; ISSN: 0739-7240
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Changes in glycosylated Hb (GHb) concns., K values (% disappearance of glucose/min after an i.v. injection of 1 g/kg dextrose), and blood glucose concns. were examd. in eight cats before and during the induction of diabetes, and in four of these cats after they were placed on insulin treatment. There was a statistically significant sepn. of GHb, K values, and fasting blood glucose concns. between healthy and diabetic cats. Changes in GHb correlated best with the K value and single weekly fasting glucose concns. averaged over eight periods for each cat while diabetes was induced ($R = 0.80$ and 0.78, resp.); however, fasting blood glucose concns. obtained on the day of the GHb measurement were also highly correlated ($R = 0.69$; $P < 0.001$). The correlation between GHb and single weekly glucose concns. obtained in insulin-treated cats at the time of insulin peak action and averaged over an 8-wk time period for each cat was less but still significant ($R = 0.53$; $P < 0.001$). It is concluded that GHb measurements are a simple and reliable way to monitor changes in glucose control in the diabetic cat over a prolonged period.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L155 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:182650 CAPLUS
DOCUMENT NUMBER: 104:182650
TITLE: Evaluation of glycosylated hemoglobin in HbA

AUTHOR(S): Masuda, Yoshinobu; Kawada, Yoichi; Nasu, Masato; Fujita, Seiichi; Tsuji, Tetsu; Katayama, Yoshiaki; Ito, Keiichi; Urata, Takayoshi; Maruyama, Nobuyuki
CORPORATE SOURCE: Natl. Cardiovascul. Cent., Suita, 565, Japan
SOURCE: Igaku no Ayumi (1985), 135(5), 429-32
CODEN: IGAYAY; ISSN: 0367-7826
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Hb A1c was detd. in human blood samples by the HPLC method of Y. Masuda et al. (1984) and glycoHb (G-Hb) was detd. by the affinity chromatog. method of D. C. Klenk et al. 1982) to study the clin. significance of G-Hb in Hb A0. G-Hbs in Hb A0 and Hb A1 were successfully detd. by the method without pretreatment for labile Hbs. The G-Hb detn. may accurately reflect the blood sugar control in diabetic patients complicated with renal insufficiency.

L155 ANSWER 19 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002153353 EMBASE
TITLE: Can glycohemoglobin be used to assess glycemic control in patients with chronic renal failure?.
AUTHOR: Little R.R.; Tennill A.L.; Rohlfing C.; Wiedmeyer H.-M.; Khanna R.; Goel S.; Agrawal A.; Madsen R.; Goldstein D.E.
CORPORATE SOURCE: R.R. Little, Department of Child Health, Univ. of Missouri School of Medicine, 1 Hospital Dr., Columbia, MO 65212, United States. LittleR@health.missouri.edu
SOURCE: Clinical Chemistry, (2002) 48/5 (784-786).
Refs: 17
ISSN: 0009-9147 CODEN: CLCHAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
027 Biophysics, Bioengineering and Medical Instrumentation
028 Urology and Nephrology
029 Clinical Biochemistry
LANGUAGE: English

L155 ANSWER 20 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97014649 EMBASE
DOCUMENT NUMBER: 1997014649
TITLE: Glycated hemoglobin and related factors in diabetic children and adolescents under 18 years of age: A Belgian experience.
AUTHOR: Dorchy H.; Roggemans M.-P.; Willems D.
CORPORATE SOURCE: Dr. H. Dorchy, Diabetology Clinic, Univ. Children's Hosp. Queen Fabiola, Avenue JJ Crocq, 15, B-1020 Brussels, Belgium
SOURCE: Diabetes Care, (1997) 20/1 (2-6).
Refs: 20
ISSN: 0149-5992 CODEN: DICAD2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
007 Pediatrics and Pediatric Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB OBJECTIVE - To determine, in an unselected population of diabetic children and adolescents .ltoreq. 18 years of age, which HbA(1c) levels can be achieved, and to examine the relationships with insulin regimen, insulin dose, sex, diabetes duration, BMI, and frequency of home blood glucose monitoring (HBGM) and outpatient clinic attendance. RESEARCH DESIGN AND METHODS - A total of 144 unselected subjects (73 boys and 71 girls) aged 11.8 .+-. 3.7 years (mean .+-. SD) were included in the study over a

6-month period. They had diabetes durations ranging from 5 months to 15 years (4.0 .+-. 3.0). They were followed by the same pediatric diabetologist and the same nurse. The yearly frequency of visits was 89 .+-. 2.0, and the monthly frequency of HBGM was 111 .+-. 27. Of the patients, 129 were treated with two daily insulin rejections of an individualized mixture of rapid- and intermediate-acting insulins, and 15 adolescents were treated with four injections using the basal-bolus regimen. The patients were divided into two subgroups according to diabetes duration: .ltoreq.2 years (n = 53) and >2 years (n = 91), i.e., outside the honeymoon period. HbA(1c) was measured by a high-pressure liquid chromatography method (normal values 3.9-5.5%). RESULTS - The mean .+-. SD HbA(1c) level in the 144 children and adolescents was 6.6 .+-. 1.2% using our method. In 62% of the patients, it was possible to obtain an HbA(1c) level under the normal mean value plus 5 SD. HbA(1c) was not related to sex, number of insulin injections, or age, i.e., it was not poorer at adolescence. The mean daily insulin dose was 0.9 U/kg body wt, being lower during the first 2 years of diabetes and reaching 1 U at adolescence HbA(1c) levels were lower during the first 2 years of diabetes (6.2 .+-. 1.0%) than afterwards (6.9 .+-. 1.2%), but the frequencies of outpatient visits and HBGM were higher. After 2 years, HbA(1c) was negatively correlated with the frequency of HBGM. The yearly incidence rate of severe hypoglycemic episodes was 0.2. After the age of 13 years, BMI was significantly higher in girls anti in adolescents on four daily injections. CONCLUSIONS - In nearly two-thirds of diabetic children and adolescents, it is possible to obtain HbA(1c) levels under the normal mean plus 5 SD, which is considered satisfactory and close to that of the adult cohort of the Diabetes Control and Complications Trial (DCCT) with intensive treatment. There is no difference between the children on only two daily insulin injections and the adolescents on four injections. After 2 years of diabetes, increased frequency of HBGM helps reduce HbA(1c) levels, taking into account the 'intensive' education of the patients and their families. Adolescent girls on four injections must pay attention to the risk of becoming overweight.

L155 ANSWER 21 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96373162 EMBASE
DOCUMENT NUMBER: 1996373162
TITLE: Relationship between grade of diabetic retinopathy and HbA(1C) values measured over the long term.
AUTHOR: Kimura M.; Kimura S.; Yoshimoto H.
CORPORATE SOURCE: Dept of Ophthalmol, Hirosaki Univ School of Med, 5 Zaifu-cho,Hirosaki 036, Japan
SOURCE: Folia Ophthalmologica Japonica, (1996) 47/11 (1350-1352). ISSN: 0015-5667 CODEN: NGKYA3
COUNTRY: Japan
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 012 Ophthalmology
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
AB To determine how progression of HbA1C values might correspond with grade of diabetic retinopathy, we performed the following study in 61 patients with non-insulin dependent diabetes mellithus. Patients were classified into three groups, according to their latest ophthalmoscopic findings: no diabetic retinopathy (NDR), simple retinopathy (SDR), and preproliferative diabetic retinopathy (PPDR). HbA(1C) values from 4 and 8 years previously were evaluated for each group and differences among the groups were evaluated by analysis of variance. The averages of the most recent HbA(1C) values for the three groups were 6.5% (NDR), 7.8% (SDR), and 7.5% (PPDR), and the differences between the groups were not significant. The averages of HbA(1C) values for 4 years previously were 6. 5% (NDR), 8.0% (SDR), and 8.8% (PPDR), and averages for values 8 years previously were 6.6%, 7. 7%, and 10.1% respectively. The differences between the NDR and PPDR group averages 4 years previously and 8 years previously and between the SDR and

PPDR groups 8 years previously were statistically significant, showing that insufficient blood glucose control affects retinopathy more than 8 years later.

L155 ANSWER 22 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95090010 EMBASE
DOCUMENT NUMBER: 1995090010
TITLE: Assessing blood glucose control in diabetes mellitus [10].
AUTHOR: Standing S.; Taylor R.; Bulusu S.; Goldie D.J.; Gunneberg A.; Kilpatrick E.S.; Rumley A.G.; Dominiczak M.H.; Small M.
CORPORATE SOURCE: Department of Clinical Biochemistry, John Radcliffe Hospital,Oxford OX3 9DU, United Kingdom
SOURCE: British Medical Journal, (1995) 310/6981 (740-741).
ISSN: 0959-8146 CODEN: BMJOAE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English

L155 ANSWER 23 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94243730 EMBASE
DOCUMENT NUMBER: 1994243730
TITLE: Is glycohemoglobin testing useful in diabetes mellitus? Lessons from the diabetes control and complications trial.
AUTHOR: Goldstein D.E.; Little R.R.; Wiedmeyer H.-M.; England J.D.; Rohlfing C.L.; Wilke A.L.
CORPORATE SOURCE: Department of Child Health, University of Missouri, Columbia School of Medicine, One Hospital Dr.,Columbia, MO 65212, United States
SOURCE: Clinical Chemistry, (1994) 40/8 (1637-1640).
ISSN: 0009-9147 CODEN: CLCHAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
029 Clinical Biochemistry
036 Health Policy, Economics and Management
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To address the question, Do laboratory tests cost money or save money? we have used as a model for discussion a common chronic disease, diabetes mellitus, and a widely used laboratory test, that for glycohemoglobin, a measure of long-term glycemia used to manage diabetic patients. Diabetes mellitus is serious, highly prevalent, and costly. In 1992, $1 of every $7 spent on health in the US was for diabetes, predominantly for treatment of the chronic complications of the disease. The recently completed Diabetes Control and Complications Trial (DCCT) demonstrated that development and progression of the chronic complications of diabetes are related to the degree of altered glycemia as quantified by determinations of glycohemoglobin. Thus, use of glycohemoglobin testing for routine diabetes care provides an objective measure of a patient's risk for developing diabetic complications. Results of this test can alert patients and health providers to the need for change in the treatment plan. Optimal use of glycohemoglobin testing for diabetes care will require standardization of test results.

L155 ANSWER 24 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94347623 EMBASE
DOCUMENT NUMBER: 1994347623
TITLE: Fructosamine and glycated haemoglobin in the assessment of long term glycaemic control in diabetes.
AUTHOR: Shield J.P.H.; Poyser I.; Hunt L.; Pennock C.A.
CORPORATE SOURCE: Institute of Child Health, St Michael's Hill,Bristol BS2

8BJ, United Kingdom
SOURCE: Archives of Disease in Childhood, (1994) 71/5 (443-445).
ISSN: 0003-9888 CODEN: ADCHAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
007 Pediatrics and Pediatric Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Fructosamine and glycated haemoglobin were measured simultaneously in 147 children with diabetes. If glycated haemoglobin is considered as the 'gold standard' for long term glycaemic control, then fructosamine is a poor indicator of actual glycated haemoglobin values, with wide 95% confidence (fiducial) limits. This shows that it is impossible to accurately predict glycated haemoglobin concentrations and therefore, by implication, longer term glycaermic control, from measurements of fructosamine. As the major studies on the prevention of microvascular complications in diabetes have used glycated haemoglobin levels to assess glycaemic control, it is suggested that this measurement should be used in all children with diabetes in preference to the measurement of fructosamine.

L155 ANSWER 25 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94044025 EMBASE
DOCUMENT NUMBER: 1994044025
TITLE: Glycated hemoglobin in the assessment of diabetes control.
AUTHOR: Daneman D.
CORPORATE SOURCE: Hospital for Sick Children, 555 University Avenue,Toronto, Ont. M5G 1X8, Canada
SOURCE: Endocrinologist, (1994) 4/1 (33-43).
ISSN: 1051-2144 CODEN: EDOCEB
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
LANGUAGE: English

L155 ANSWER 26 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91220929 EMBASE
DOCUMENT NUMBER: 1991220929
TITLE: Comparison of the real-time use of glycosylated haemoglobin and plasma fructosamine in the diabetic clinic.
AUTHOR: Watts G.F.; Macleod A.F.; Benn J.J.; Slavin B.M.; Morris R.W.; Williams C.D.; Kearney E.M.; Lowy C.; Sonksen P.H.
CORPORATE SOURCE: Dept. Endocrinology/Chem. Path, UMDS, St Thomas' Hospital,London SE1 7EH, United Kingdom
SOURCE: Diabetic Medicine, (1991) 8/6 (573-579).
ISSN: 0742-3071 CODEN: DIMEEV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The within-clinic use of glycosylated haemoglobin (HbA1) and plasma fructosamine results in assessing blood glucose control and clinical management was compared in 1030 diabetic patients. The physician initially reviewed the patient with one randomly allocated measure (HbA1 or fructosamine) and completed a questionnaire concerning perception of blood glucose control, alteration to diet, alteration to medication, referral for diabetes education, and follow-up interval. The patient was then re-assessed using the second measure and the questionnaire repeated. Discordance rates for the study end-points, judged as binary outcomes,

were: blood glucose control 15%; alteration to diet 7%; alteration to medication 9%; referral for education 3%; follow-up interval 4%. A significantly greater number of patients were rated as poorly controlled with HbA1 than with fructosamine ($p < 0.001$) and were, in consequence, more frequently recommended alteration to diet and medication, referral for education and shorter follow-up interval; the rate of discordance for at least one of the management decisions was 16%. Multifactorial analysis showed that discordant management was dependent on the reviewing physician ($p < 0.001$) and a history of cardiovascular disease ($p < 0.01$); but neither type of diabetes, nor presence of nephropathy or variant haemoglobins, nor plasma glucose concentration, significantly influenced the likelihood of a discordance. Replacing HbA1 with fructosamine in the diabetic clinic may result in significant differences in the physician's perception of blood glucose control and in the management of patients.

L155 ANSWER 27 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90376025 EMBASE
DOCUMENT NUMBER: 1990376025
TITLE: Within-clinic glycosylated haemoglobin measurement.
AUTHOR: Rumley A.G.; Carlton G.; Small M.
CORPORATE SOURCE: Dept. of Biochemistry, Gartnavel General Hospital,Glasgow G12 0YN, United Kingdom
SOURCE: Diabetic Medicine, (1990) 7/9 (838-840).
ISSN: 0742-3071 CODEN: DIMEEV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The performance of the Diamat HPLC analyser (Bio Rad Instruments) was assessed, and the effect of this on-site HbA1 assay on the therapeutic decisions made at the diabetic clinical evaluated. The intra-assay CV for HbA1 at concentrations of 8.3 and 13.4% was 3.8 and 0.4%, respectively, with inter-assay CV of 5.0 and 3.0%. On a single day 82 HbA1 tests on consecutive patients were performed at the clinic. In 43 insulin-treated patients and 79 non-insulin-treated diabetic patients the HbA1 result changed the management decision in 25 and 18% of patients, respectively. The relationship between HbA1 and self blood glucose monitoring (SBGM) results in the previous 6-week period were also evaluated. In 41% of patients with insulin-treated diabetes who produced SBGM diaries there was a discrepancy between categories of blood glucose control, all of these patients having better SBGM than HbA1 values. This study highlights the feasibility and value of a within-clinic HbA1 assay for clinical decision-making and its usefulness in identifying problems of agreement with self-monitored cells.

L155 ANSWER 28 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90027252 EMBASE
DOCUMENT NUMBER: 1990027252
TITLE: Radioimmunoassay of glycated serum protein using monoclonal antibody to glucitollysine and Coomassie-Brilliant-Blue-coated polystyrene beads.
AUTHOR: Yamamoto Y.; Tahara Y.; Cha T.; Noma Y.; Fukuda M.; Yamato E.; Yoneda H.; Hashimoto F.; Ohboshi C.; Hirota M.; Iida M.; Shin S.; Shima K.
CORPORATE SOURCE: Dept. of Geriatric Medicine, Osaka University, Medical School,Fukushima-ku, Osaka 553, Japan
SOURCE: Diabetes Research, (1989) 11/1 (45-49).
ISSN: 0265-5985 CODEN: DIREEM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A radioimmunoassay for glycated serum protein (GSP) was developed using monoclonal antibody to glucitollysine and polystyrene beads coated with Coomassie-Brilliant-Blue (CBB) as adsorbent for serum protein. The monoclonal antibody was raised by immunizing BALB/c mice with reduced glycated LDL and fusing their spleen cells with mouse myeloma cells. CBB-coated polystyrene beads were introduced to absorb a constant amount of serum protein. The protein adsorbed on the CBB-coated beads was reduced by NaHB4, and after treatment with radiolabeled antibody, the radioactivity of each bead was counted with an automatic .gamma.-counter. The standard glycated protein used was reduced glycated human serum albumin, in which 8 of 59 lysine residues were glycated. The intra- and interassay coefficients of variation of GSP were 4.8-6.5% and 1.6-6.0%, respectively. The GSP level of diabetic patients was significantly higher than that of normal controls (1.97 .+-. 12.3 vs. 0.47 .+-. 0.21 nmol/mg-protein; mean .+-. SD, $p < 0.001$). The GSP levels of patients with insulin-dependent and non-insulin-dependent diabetes mellitus were 3.03 .+-. 1.05 and 1.51 .+-. 1.00 nmol/mg-protein, respectively. A good correlation was found between the levels of GSP and hemoglobin A1c (HbA1c) ($r = 0.85$, $p < 0.001$). In patients admitted to the hospital for diabetes education and glycemic control, the GSP level decreased 43 .+-. 12% with the decrease in the fasting plasma glucose level (39 .+-. 13%) and the mean daily plasma glucose level (MPG, 47 .+-. 15%) in a four week period after admission, whereas the HbA1c level decreased only 13 .+-. 6% during this period. The correlation coefficients of the level of GSP with that of MPG measured 0 (same day), 1, 2, 3 and 4 weeks before the day of measurement of GSP were 0.66, 0.62, 0.60, 0.59 (all $p < 0.001$) and 0.46 ($p < 0.05$), respectively. These data suggest that the present radioimmunoassay system is useful for evaluation of glycemic control in a much shorter period than that required for evaluation by measurement of HbA1c.

L155 ANSWER 29 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-013543 [02] WPIDS
DOC. NO. NON-CPI: N2002-010957
DOC. NO. CPI: C2002-003694
TITLE: Hemoglobin measurement by cation exchange liquid chromatography, involves eluting hemoglobin in specific order, and setting eluant conditions, to get preset separation degree between maximum contiguity hemoglobin peaks.
DERWENT CLASS: B04 **S03**
PATENT ASSIGNEE(S): (SEKI) SEKISUI CHEM IND CO LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 2001228133 A		20010824	(200202)*		13

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2001228133 A		JP 2000-41181	20000218

PRIORITY APPLN. INFO: JP 2000-41181 20000218
AB JP2001228133 A UPAB: 20020109

NOVELTY - Measurement of hemoglobin (Hb) by cation exchange liquid chromatography, involves eluting Hb in an order of HbA1a, HbA1b, HbF, unstable type **HbA1c** (L-**HbA1c**), stable type **HbA1c** (S-**HbA1c**), and HbA0. The eluant conditions are set up, so that the degree of separation between the maximum contiguity peaks of each peak of HbA1a, HbA1b and HbF, is 0.8 or less.

USE - For measuring hemoglobin, such as stable type hemoglobin A1c, by cation exchange liquid chromatography, for measuring blood glucose level in diabetic screening test and diabetic patients, useful for **controlling** blood **glucose** level.

ADVANTAGE - The method enables efficient and highly accurate measurement of hemoglobin (Hb), preferably stable type **HbA1c**, which is less than half of the time required conventionally. The test substance measuring time for 1 elute is efficiently reduced to 60% or less, when compared conventionally.

Dwg.0/12

L155 ANSWER 30 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-349398 [30] WPIDS
DOC. NO. NON-CPI: N2000-261755
DOC. NO. CPI: C2000-106133
TITLE: Biosensor for measuring levels of glycoprotein and **glycosylated hemoglobin** in whole blood, useful in the **control** of **diabetes**.
DERWENT CLASS: A96 B04 **S03**
INVENTOR(S): SHIEH, P
PATENT ASSIGNEE(S): (SHIE-I) SHIEH P
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6054039	A	20000425	(200030)*		15

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6054039	A	US 1997-914283	19970818

PRIORITY APPLN. INFO: US 1997-914283 19970818
AB US 6054039 A UPAB: 20000624

NOVELTY - The levels of glycoprotein and **glycosylated hemoglobin** in blood can be measured using amperometric biosensors, useful for patients with diabetes.

DETAILED DESCRIPTION - An amperometric sensor for assaying the concentration of a fructosamine moiety in a biological fluid in the presence of interfering oxidizable substances comprises:

(a) a sensing electrode, comprising a non-conductive support strip coated with a conductive layer containing a first redox mediator;

(b) a reference electrode comprising a non-conductive support strip coated with a conductive formulation comprising Ag/AgCl dispersed in a resin formulation, and with the reference electrode having an opening;

(c) a reagent strip comprising a water absorbent carrier impregnated with a mixture comprising a second redox mediator that can be reduced by a fructosamine derivative, at least one surfactant, at least one stabilizer, a buffering agent to maintain pH of 8-12; and

(d) a whole blood treatment component selected from an erythrocyte filtration component and an erythrocyte lysing component.

The conductive layers of each electrode face each other, the reagent strip is superimposed on the conducting layer of the sensing electrode, the whole blood treatment component is superimposed on the reagent strip;

the conductive layer of the reference electrode is superimposed on the whole blood treatment component; the whole blood treatment component completely covers the opening in the reference electrode, so that the sensing electrode, the reagent strip, the whole blood treatment component and the reference electrode form a sandwich.

An INDEPENDENT CLAIM is made for the amperometric determination of the concentration of **glycosylated hemoglobin** by using a first biosensor with an erythrocyte filtration component, and a second biosensor comprising an erythrocyte lysing component; measuring the current passing between the sensing and reference electrodes in each biosensor to give the concentration of fructosamine measured by each biosensor; subtracting the concentration given by the biosensor with the filtration component from the concentration given by the biosensor with the lysing component to obtain the concentration of **glycosylated hemoglobin** in whole blood.

USE - For monitoring diabetes.

ADVANTAGE - The biosensor is easily miniaturized, needs only small test samples, and produces rapid and accurate results.

Dwg.0/5

L155 ANSWER 31 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-001547 [01] WPIDS
DOC. NO. NON-CPI: N1999-001365
DOC. NO. CPI: C1999-000511
TITLE: **Control** of **diabetes** and monitoring effectiveness of treatment - comprises predicting level of **glycosylated haemoglobin** in blood using known blood glucose and **glycosylated haemoglobin** levels.
DERWENT CLASS: B04 P31 **S03**
INVENTOR(S): HEINONEN, P; MAEKIPAEAE, M
PATENT ASSIGNEE(S): (OYNO) NOKIA MOBILE PHONES LTD
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 881495	A1	19981202	(199901)*	EN	15
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
FI 9702292	A	19981201	(199910)		
JP 10332704	A	19981218	(199910)		11
KR 98087191	A	19981205	(200009)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 881495	A1	EP 1998-660040	19980506
FI 9702292	A	FI 1997-2292	19970530
JP 10332704	A	JP 1998-147378	19980528
KR 98087191	A	KR 1998-18039	19980519

PRIORITY APPLN. INFO: FI 1997-2292 19970530
AB EP 881495 A UPAB: 19990107

Control of **diabetes** and measurement of effectiveness of treatment is based on a mathematical model derived from the behaviour of a **glycosylated haemoglobin** component level relative to the blood glucose level using previously measured levels. The model is updated when a new **glycosylated haemoglobin** component level is measured using that measure and recent new blood glucose level measurements. The model is used to predict the **glycosylated**

haemoglobin component level, between measurements of that level, using measurements of the blood glucose level obtained since the last **glycosylated haemoglobin** component measurement.

ADVANTAGE - Blood glucose levels are easily measured in the patient's home. The **glycosylated haemoglobin** content is much more difficult to measure and is usually only tested every three to four months. The present method correlates the two measurements, and so the blood glucose level can be used to predict the **glycosylated haemoglobin** content for continuous monitoring of the diabetic condition.

Dwg.0/6

L155 ANSWER 32 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1996-386426 [39] WPIDS
DOC. NO. NON-CPI: N1996-325657
DOC. NO. CPI: C1996-121683
TITLE: Reagents for determining total haemoglobin content - and opt. content of particular haemoglobin deriv. in blood samples, comprise haemolysis reagent and green chromophore-forming reagent.
DERWENT CLASS: A96 B04 D16 **S03**
INVENTOR(S): BONA, V; VORBERG, E; WITZIGMANN, A
PATENT ASSIGNEE(S): (HOFF) HOFFMANN LA ROCHE & CO AG F
COUNTRY COUNT: 17
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 729031	A1	19960828	(199639)*	EN	10
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT					
CA 2169882	A	19960825	(199651)		
JP 08262027	A	19961011	(199651)		10

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 729031	A1	EP 1996-102222	19960215
CA 2169882	A	CA 1996-2169882	19960220
JP 08262027	A	JP 1996-36873	19960223

PRIORITY APPLN. INFO: EP 1995-102635 19950224
AB EP 729031 A UPAB: 19961004
The following are claimed:

(A) a set of reagents for determining the content of total haemoglobin (Hb) in blood samples (or samples derived from blood), comprising:

(a) a haemolysis reagent which is an acidic soln. having a pH of 0.5-5.0, esp. 0.5-3.0 and

(b) a green chromophore forming reagent which is a basic soln. (having a pH of 7.0-12.0 (esp. 0.9-11.5)) contg. a nonionic detergent and/or an ionic detergent;

(B) a set of reagents for determining both the content of total Hb and the content of a particular Hb deriv. in a blood sample (or sample derived from blood), comprising:

(a') a haemolysis reagent as described above,

(b') a green chromophore forming reagent as described above and

(c') a reagent for determining the content of a particular Hb deriv.;

(C) determining the content of total Hb in a blood sample (or sample derived from blood) comprising:

(a'') treating the sample with a haemolysis reagent as described in (A) above and

(b'') incubating the resulting haemolysate with a green chromophore forming reagent (as described in (A) above) for a sufficient period of time so as to convert all Hb derivs. into a green chromophore, and measuring the absorbance of the soln. obtd., and

(D) determining both the content of total Hb and the content of a particular Hb deriv., in a blood sample (or sample derived from blood), comprising:

(a''') treating the sample with a haemolysis reagent as described in (A) above,

(b''') incubating an aliquot of the resulting haemolysate with a green chromophore forming reagent (as described in (A) above) for a sufficient period of time so as to convert all Hb derivs. into a green chromophore, and measuring the absorbance of the soln. obtd. and

(c''') determining the content of the particular Hb deriv. in another aliquot of the haemolysate.

USE - The reagents are particularly useful for the determination of the content of glycated Hb derivs. such as HbA1a, HbA1b and **HbA1c** . The ratio between the content of a particular glycated Hb deriv. and the content of total Hb reflects the average glucose level in blood and is thus a parameter for monitoring metabolic **control** in **diabetes.**

ADVANTAGE - The processes allow the determination of the content of total Hb and the content of a particular Hb deriv. and can thus yield the ratio described under 'use' above.

Dwg.0/2

L155 ANSWER 33 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1990-361604 [48] WPIDS
DOC. NO. NON-CPI: N1990-275887
DOC. NO. CPI: C1990-157179
TITLE: Assaying **glycosylated haemoglobin** without sepn. from haemoglobin - by reaction with specific labelling cpd. contg. di hydroxy boryl gps., sepn. of total haemoglobin and measuring bound label.
DERWENT CLASS: B04 D16 **S03**
INVENTOR(S): SUNDREHAGEN, E; HOLMES, M J
PATENT ASSIGNEE(S): (AXIS-N) AXIS RES AS; (AXIS-N) AXIS BIOCHEMICALS AS
COUNTRY COUNT: 25
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9013818	A	19901115	(199048)*		47
RW: AT BE CH DE DK ES FR GB IT LU NL SE					
W: AU BR CA FI HU JP KR NO RO SU US					
AU 9056670	A	19901129	(199109)		
FI 9105284	A	19911108	(199207)		
EP 471774	A	19920226	(199209)		47
R: AT BE CH DE ES FR GB IT LI LU NL SE					
NO 9104372	A	19920109	(199214)		
BR 9007357	A	19920421	(199231)		
JP 04506703	W	19921119	(199301)		17
US 5242842	A	19930907	(199337)		13
AU 642879	B	19931104	(199351)		
EP 471774	B1	19950125	(199508)	EN	23
R: AT BE CH DE DK ES FR GB IT LI LU NL SE					
HU 66835	T	19950130	(199510)		
DE 69016423	E	19950309	(199515)		
ES 2067029	T3	19950316	(199517)		
JP 08012196	B2	19960207	(199610)		14
FI 100437	B1	19971128	(199802)		
NO 302784	B1	19980420	(199823)		
HU 215181	B	19981028	(199850)		

RU 2111494 C1 19980520 (199850)
KR 9610697 B1 19960807 (199923)
CA 2055430 C 19990831 (200002) EN

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 471774	A	EP 1990-908231	19900511
NO 9104372	A	NO 1989-1929	19890511
BR 9007357	A	BR 1990-7357	19900511
		WO 1990-EP820	19900511
JP 04506703	W	JP 1990-507703	19900511
		WO 1990-EP820	19900511
US 5242842	A	WO 1990-EP820	19900511
		US 1990-613505	19901101
AU 642879	B	AU 1990-56670	19900511
EP 471774	B1	EP 1990-908231	19900511
		WO 1990-EP820	19900511
HU 66835	T	HU 1990-4320	19900511
		WO 1990-EP820	19900511
DE 69016423	E	DE 1990-616423	19900511
		EP 1990-908231	19900511
		WO 1990-EP820	19900511
ES 2067029	T3	EP 1990-908231	19900511
JP 08012196	B2	JP 1990-507703	19900511
		WO 1990-EP820	19900511
FI 100437	B1	WO 1990-EP820	19900511
		FI 1991-5284	19911108
NO 302784	B1	WO 1990-EP820	19900511
		NO 1991-4372	19911108
HU 215181	B	HU 1990-4320	19900511
		WO 1990-EP820	19900511
RU 2111494	C1	SU 1990-5010459	19900511
		WO 1990-EP820	19900511
KR 9610697	B1	WO 1990-NO4	19900104
		WO 1990-EP820	19900511
		KR 1991-701571	19911109
CA 2055430	C	CA 1990-2055430	19900511
		WO 1990-EP820	19900511

FILING DETAILS:

PATENT NO	KIND		PATENT NO
BR 9007357	A	Based on	WO 9013818
JP 04506703	W	Based on	WO 9013818
US 5242842	A	Based on	WO 9013818
AU 642879	B	Previous Publ.	AU 9056670
		Based on	WO 9013818
EP 471774	B1	Based on	WO 9013818
HU 66835	T	Based on	WO 9013818
DE 69016423	E	Based on	EP 471774
		Based on	WO 9013818
ES 2067029	T3	Based on	EP 471774
JP 08012196	B2	Based on	JP 04506703
		Based on	WO 9013818
FI 100437	B1	Previous Publ.	FI 9105284
NO 302784	B1	Previous Publ.	NO 9104372
HU 215181	B	Previous Publ.	HU 66835
		Based on	WO 9013818
CA 2055430	C	Based on	WO 9013818

PRIORITY APPLN. INFO: NO 1989-1929 19890511; WO 1990-NO4 19900104

AB WO 9013818 A UPAB: 19950301

Glycoslylated haemoglobin (gHb) is assessed in a sample by (1) opt. haemolysing the sample to release any cell-bound Hb; (2) reacting with a signal-forming molecule (I) consisting fo one or more dihydroxyboryl residues (or their salts) linked to a signal-forming label (A); (3) sepg. gHb and non-**glycosylated Hb** (ngHb), and any molecules bound to them and (4) assessing (A) bound to the sepd. Hb and/or any non-Hb bound (I). Opt. step (3) can precede step (2).

Also new are (I) consisting of a conjugate of the dihydroxyboryl residues with a radioactive or chemiluminescent. Specifically (I) is not immobilised and steps (2) and (3) can be carried out simultaneously. The amts. of both gHb and ngHb are assessed and total Hb is pptd. selectively by addn. of Zn and/or Cu ions, opt. together with a metal-complexing agent.

USE/ADVANTAGE - The method is used to diagnose and monitor diabetes mellitus, esp. to evaluate long-term **control** of blood **glucose**. It is specific, rapid, simple and readily adapted for use in clinical laboratories. No sepn. of gHb and ngHb is required. @(47pp Dwg.No.1/3)@

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L155 ANSWER 34 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1986-299732 [46] WPIDS
DOC. NO. NON-CPI: N1986-224026
DOC. NO. CPI: C1986-129854
TITLE: Determination of glycated haemoglobin in blood - using monoclonal antibody showing preferential binding to human **HbA1c**.
DERWENT CLASS: B04 D16 **S03**
INVENTOR(S): KRUSE, V; PRENTO, A; ZEUTHEN, J; PRENTOE, A
PATENT ASSIGNEE(S): (NOVO) NOVO NORDISK A/S; (NOVO) NOVO INDUSTRI A/S; (NOVO) NOVO IND AS
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 201187	A	19861112	(198646)*	EN	34
R: AT BE CH DE FR GB IT LI LU NL SE					
AU 8655321	A	19861002	(198652)		
FI 8601358	A	19860930	(198703)		
JP 61280571	A	19861211	(198704)		
DK 8601299	A	19860930	(198714)		
PT 82296	A	19870506	(198722)		
ES 8800351	A	19880101	(198809)		
EP 201187	B	19920122	(199204)		
R: AT BE CH DE FR GB IT LI LU NL SE					
DE 3683532	G	19920305	(199211)		
US 5206144	A	19930427	(199318)		12
FI 89379	B	19930615	(199328)		
JP 07020437	B2	19950308	(199514)		11

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 201187	A		EP 1986-302372	19860327
JP 61280571	A		JP 1986-70649	19860328
ES 8800351	A		ES 1986-553472	19860326
US 5206144	A	Cont of	US 1986-844854	19860327
		Cont of	US 1988-248250	19880919

		US 1990-607766	19901030
FI 89379	B	FI 1986-1358	19860327
JP 07020437	B2	JP 1986-70649	19860328

FILING DETAILS:

PATENT NO	KIND		PATENT NO
FI 89379	B	Previous Publ.	FI 8601358
JP 07020437	B2	Based on	JP 61280571

PRIORITY APPLN. INFO: DK 1985-1453 19850329; DK 1986-1299 19860321

AB EP 201187 A UPAB: 19930922
Monoclonal antibody of rodent origin exhibits a preferential binding to human **HbA1c** as compared with its binding to human HbAo. It pref. binds to an epitope of **HbA1c** which comprises the glycated amino gp. of the N-terminal valine of the haemoglobin A beta-chain. The antibody may be obtd. from the hybridoma cell line HEM 13F1 or a reclone thereof e.g. HEM 13F1A4.

The antibody is prepd. by (a) immunising a rodent, pref. mouse, with **HbA1c**, (b) immortalising the antibody producing cells by fusing them with myeloma cells to produce hybridoma cells, (c) selecting by differential screening hybridoma cells which produce an antibody showing a preferential binding to **HbA1c**, glycated at the N-terminal valine of the beta-chains and possibly contg. additional glycated lysine residues, was purified by conventional procedures such as cation exchange chromatography or HPLC.

USE - The monoclonal antibody can be used as a diagnostic aid for the determination of glycated human haemoglobin as an index for an individuals glycemic control.

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L155 ANSWER 35 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1986-162357 [26] WPIDS
CROSS REFERENCE: 1989-292825 [41]
DOC. NO. NON-CPI: N1986-120977
DOC. NO. CPI: C1986-069548
TITLE: Specific immunoassay for denatured protein analyte - by reaction with antibody specific for linear peptide epitope, esp. for assay of glucosylated haemoglobin.
DERWENT CLASS: B04 D16 **S03**
INVENTOR(S): HAIGH, W; KNOWLES, W; MARCHEST, V; KNOWLES, W J; MARCHESI, V T; MARCHESI, V
PATENT ASSIGNEE(S): (MOLE-N) MOLECULAR DIAGNOSTICS INC; (MILE) MILES INC; (FARB) BAYER CORP
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
AU 8549260	A	19860508	(198626)*		69
DK 8504940	A	19860430	(198630)		
ZA 8508251	A	19860505	(198632)		
FI 8504187	A	19860430	(198636)		
JP 61172064	A	19860802	(198637)		
EP 185870	A	19860702	(198639)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE					
US 4647654	A	19870303	(198711)		
US 4658022	A	19870414	(198717)		
ES 8705633	A	19870716	(198733)		
ES 8800435	A	19880101	(198809)		
US 4727036	A	19880223	(198811)		

EP 316306	A	19890517 (198920)	EN		
R: AT BE CH DE FR GB IT LI LU NL SE					
FI 9004226	A	19900827 (199049)			
IL 76827	A	19901129 (199105)			
IL 91034	A	19901129 (199105)			
DK 9101307	A	19910704 (199145)			
EP 185870	B1	19920923 (199239)	EN	26	
R: AT BE CH DE FR GB IT LI LU NL SE					
DE 3586679	G	19921029 (199245)			
EP 316306	B1	19931215 (199350)	EN	25	
R: AT BE CH DE FR GB IT LI LU NL SE					
DE 3587687	G	19940127 (199405)			
DK 167825	B	19931220 (199405)			
JP 07023891	B2	19950315 (199515)		20	
JP 07051087	A	19950228 (199517)		19	
IE 63731	B	19950614 (199531)			
IE 63768	B	19950614 (199531)			
EP 185870	B2	19980617 (199828)	EN		
R: AT BE CH DE FR GB IT LI LU NL SE					
CA 1339952	C	19980714 (199839)			
JP 2858534	B2	19990217 (199912)		19	
FI 104376	B1	20000114 (200009)			

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
AU 8549260	A		AU 1985-49260	19851031
ZA 8508251	A		ZA 1985-8251	19851028
JP 61172064	A		JP 1985-240703	19851029
EP 185870	A		EP 1985-113157	19851017
US 4647654	A		US 1985-763193	19850808
US 4658022	A		US 1985-779730	19850927
ES 8705633	A		ES 1985-548270	19851028
ES 8800435	A		ES 1986-556865	19860701
EP 185870	B1		EP 1985-113157	19851017
DE 3586679	G		DE 1985-3586679	19851017
			EP 1985-113157	19851017
EP 316306	B1	Related to	EP 1985-113157	19851017
			EP 1989-100369	19851017
DE 3587687	G		DE 1985-3587687	19851017
			EP 1989-100369	19851017
DK 167825	B		DK 1985-4940	19851028
JP 07023891	B2		JP 1985-240703	19851029
JP 07051087	A	Div ex	JP 1985-240703	19851029
			JP 1994-18988	19851029
IE 63731	B		IE 1985-2655	19851025
IE 63768	B	Div ex	IE 1985-2655	19851025
			IE 1993-440	19851025
EP 185870	B2		EP 1985-113157	19851017
		Related to	EP 1989-100369	19851017
CA 1339952	C		CA 1985-492444	19851008
JP 2858534	B2	Div ex	JP 1985-240703	19851029
			JP 1994-18988	19851029
FI 104376	B1	Div ex	FI 1985-4187	19851025
			FI 1990-4226	19900827

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 3586679	G	Based on	EP 185870
DE 3587687	G	Based on	EP 316306

DK 167825	B	Previous Publ.	DK 8504940
JP 07023891	B2	Based on	JP 61172064
EP 185870	B2	Related to	EP 316306
JP 2858534	B2	Previous Publ.	JP 07051087
FI 104376	B1	Previous Publ.	FI 9004226

PRIORITY APPLN. INFO: US 1984-665811 19841029; US 1985-763193 19850808; US 1985-779730 19850927; US 1985-779731 19850927

AB AU 8549260 A UPAB: 20000218

Immunoassay for detecting a protein analyte (I) in an aq. test sample comprises (1) denaturing protein in the test sample; (2) reacting the denatured sample with an antibody (Ab) specific for binding a linear peptide epitope in (I) and (3) determining the binding of Ab.

Pref. the epitope is inaccessible to Ab binding in the native protein. Also new are (1) monoclonal Ab (MAb), or their fragments, which bind specifically to the glucosylated N-terminal region of human haemoglobin (HHb) beta-subunit and (2) hybridoma cells which produce MAB.

USE - The method is esp. used to assay glucosylated Hb in blood (for assessing **glucose** level **control** in diabetics).

Dwg.0/9

Dwg.0/9

L155 ANSWER 36 OF 37 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:	1983-801135 [43] WPIDS
DOC. NO. NON-CPI:	N1983-192240
DOC. NO. CPI:	C1983-104716
TITLE:	Sepn. of haemoglobin A1 in lysed human blood with exchange resins - with di hydroxy-boryl cpd. in haemolysate or buffer for improved results.
DERWENT CLASS:	A96 B04 J04 **S03**
INVENTOR(S):	HANAMOTO, M S; TANAKA, S K
PATENT ASSIGNEE(S):	(BIRA) BIO RAD LAB INC
COUNTRY COUNT:	4

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 4409335	A	19831011	(198343)*		6
DE 3316452	A	19831201	(198349)		
GB 2121170	A	19831214	(198350)		
JP 58210024	A	19831207	(198404)		
GB 2121170	B	19850710	(198528)		
DE 3316452	C	19870226	(198708)		
JP 01035302	B	19890725	(198933)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 3316452	A	DE 1983-3316452	19830505
GB 2121170	A	GB 1983-13981	19830520
JP 58210024	A	JP 1982-234944	19821224

PRIORITY APPLN. INFO: US 1982-382899 19820528

AB US 4409335 A UPAB: 19930925

Sepn. of haemoglobin A1 (I) from non-**glycosylated haemoglobins** (II) and the Schiff base precursors to (I) in a human blood sample comprises (1) lysis of the red blood cells to form a haemolysate; (2) impregnation of a weak cation-exchange resin with the haemolysate; and (3) passage through the resin of a buffer contg. alkali metal ions at 0.06-0.11M to dissociate the precursors into glucose and

haemoglobin A and to elute preferentially the glucose and (I), then the eluate is recovered. A dihydroxyboryl cpd. (III) is included in the haemolysate and/or buffer.

The (I) concn. of human blood is determined without interference from the precursors. The (I) concn. is used in the diagnosis and **control** of **diabetes**.

0/0

L155 ANSWER 37 OF 37 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1980-04058C [03] WPIDS
TITLE: Sepg. glyco protein from other proteins - by complexing with support having di hydroxy boronyl gps., esp. for blood analysis.
DERWENT CLASS: A96 B04 **S03 S05**
INVENTOR(S): BOURIOTIS, V; BROWN, P J; DEAN, P D G
PATENT ASSIGNEE(S): (AMIC) AMICON CORP; (PIEC) PIERCE CHEM CO
COUNTRY COUNT: 6
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
GB 2024829	A	19800116	(198003)*		
NL 7906392	A	19810226	(198111)		
DE 2933832	A	19810326	(198114)		
FR 2464475	A	19810410	(198122)		
JP 56040694	A	19810416	(198123)		
US 4269605	A	19810526	(198124)		
GB 2024829	B	19820804	(198231)		
DE 2933832	C	19880707	(198827)		

PRIORITY APPLN. INFO: GB 1979-22367 19790627
AB GB 2024829 A UPAB: 19930902

Glycoproteins (A) are sepd. from non-glycosylated proteins by treating their mixt. with a reagent (B) contg. a dihydroxyboryl gp. bonded, pref. covalently, to a support. The resulting (A)-dihydroxyboryl complex is then sepd.

Esp. (A) is **glycosylated haemoglobin** (A') and the support is agarose which has been reacted sequentially with a 3-6C aliphatic diepoxide and an aminophenylboronic acid.

Used esp. for assaying (A') in blood (to monitor **diabetes control**) by lysing a blood sample, removing cell debris, then treated the lysed sample with (B). (A') is then pref. measured colorimetrically. The method is also useful for preparative isolation of (A). Method is rapid and does not require exact control of pH and ionic strength.

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